Absolute stereochemistry.

RN 204072-50-4 HCAPLUS CN D-Proline, 1-[(4-bromophenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-51-5 HCAPLUS
CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-hydroxy-, methyl ester,
(4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 204072-47-9 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester,
(4R)- (9CI) (CA INDEX NAME)

RN 204072-42-4 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-44-6 HCAPLUS CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-45-7 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 204072-38-8 HCAPLUS

CN D-Proline, 4-[(2-methoxyethoxy)methoxy]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-39-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-, methyl ester, (3S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 204072-41-3 HCAPLUS

CN D-Proline, 4-ethyl-4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 204072-34-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-36-6 HCAPLUS

CN D-Proline, 4-(ethoxymethoxy)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-37-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(phenylmethoxy)methoxy]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 204072-30-0 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(phenylthio)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-31-1 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)oxy]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-32-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-27-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(phenylmethoxy)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-28-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(phenylamino)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-29-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN204072-24-2 HCAPLUS

D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-CN yl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

204072-25-3 HCAPLUS D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-CNyl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN204072-26-4 HCAPLUS

D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-phenoxy-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

RN 204072-21-9 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-23-1 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 204072-20-8 HCAPLUS
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(trifluoromethyl)sulfonyl]oxy
]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 203994-82-5 HCAPLUS
CN D-Proline, 4-(acetylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,
(4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 203934-42-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 203934-63-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 203994-80-3 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Ward 10 663042

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N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[((2R)-1-oxo-2-
benzyloxypropyl)amino]pyrrolidine 204072-83-3P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[(2R)-1-oxo-2-
benzyloxy-3-phenylpropyl]amino]pyrrolidine 204072-84-4P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-
benzyloxypropyl]propylamino]pyrrolidine 204072-85-5P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-
hydroxypropyl]propylamino]pyrrolidine 204072-86-6P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-((2R)-1-oxo-2-
benzyloxy-3-phenylpropyl) propylamino] pyrrolidine 204072-87-7P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-((2R)-1-oxo-2-
hydroxy-3-phenylpropyl)propylamino]pyrrolidine 204072-88-8P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-
piperidyl)pyrrolidine 204072-89-9P, N-(4-Butoxyphenylsulfonyl)-
(2R) -methoxycarbonyl-(4S)-(1-piperidyl)pyrrolidine 204072-90-2P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
morpholinopyrrolidine 204072-91-3P, N-(4-Butoxyphenylsulfonyl)-
(2R) -methoxycarbonyl-(4S) -morpholinopyrrolidine 204072-92-4P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-
dioxothiomorpholino) pyrrolidine 204072-93-5P,
N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-
dioxothiomorpholino)pyrrolidine 204073-01-8P
537704-28-2P 537704-31-7P, N-(4-Methoxyphenylsulfonyl)-
(2R) -methoxycarbonyl-(4S) -aminopyrrolidine formate 537704-32-8P,
N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[(N-methyl-3-
imidazolyl)sulfonyl]amino]pyrrolidine 537704-35-1P
537704-63-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
(4S) - (2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-66-8P
, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,5-dioxo-1-
methylimidazolidin-3-yl)pyrrolidine 537704-68-0P,
N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-allyl-2,5-
dioxoimidazolidin-3-yl)pyrrolidine 537704-72-6P,
N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,4-dioxo-5,5-
dimethylimidazolidin-1-yl)pyrrolidine 537704-74-8P,
N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(5S)-5-methyl-2,4-
dioxoimidazolidin-1-yl]pyrrolidine 537704-76-0P,
N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-methoxycarbonyl-(4S)-(3-methyl-
2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-78-2P,
N-(4-Phenoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-methyl-2,4-
dioxoimidazolidin-1-yl)pyrrolidine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
   (intermediate; preparation of substituted cyclic amines as metalloprotease
   inhibitors for treating conditions characterized by excess
activity of these enzymes) 57850-07-4 HCAPLUS
D-Proline, 4-hydroxy-1-[(4-methylphenyl)sulfonyl]-, methyl ester, (4R)-
       (CA INDEX NAME)
```

Absolute stereochemistry.

RN

CN

```
Methoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4R) -ethoxymethoxypyrrolidine
204072-37-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
(4R) -benzyloxymethoxypyrrolidine 204072-38-8P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[(2-
methoxyethoxy) methoxy] pyrrolidine 204072-39-9P
204072-41-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
(4R) -4-hydroxy-4-ethylpyrrolidine 204072-42-4P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-4-hydroxy-4-
phenylpyrrolidine 204072-44-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-3,3-dimethyl-4-oxopyrrolidine 204072-45-7P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-3,3-dimethyl-(4R)-
hydroxypyrrolidine 204072-46-8P, N-(3,4-Dimethoxyphenylsulfonyl)-
(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-47-9P,
N-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine 204072-49-1P, N-(4-Butoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-benzoyloxypyrrolidine 204072-50-4P,
N-(4-Bromobenzenesulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine
204072-51-5P, N-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-
methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-52-6P,
N-(2,4-Dichlorophenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine 204072-55-9P, N-(4-Phenoxyphenylsulfonyl)-
(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-56-0P,
N-(4-Isobutyloxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine 204072-57-1P, N-(2-Methyl-4-
bromophenylsulfonyl) - (2R) -methoxycarbonyl - (4S) - (3-
methoxyphenylthio)pyrrolidine 204072-58-2P, N-(4-
Butoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4S) - (2-
benzothiazolylthio)pyrrolidine 204072-59-3P,
N-(2-Nitro-4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-
benzothiazolylthio)pyrrolidine 204072-60-6P,
N-(4-Butoxyphenylsulfonyl)-(2R)-Methoxycarbonyl-(4S)-(4-
methoxyphenylthio)pyrrolidine 204072-61-7P, N-(4-
Butoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4S) - (3-pyridyloxy)pyrrolidine
204072-62-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
(4S)-azidopyrrolidine 204072-64-0P, N-(4-Butoxyphenylsulfonyl)-
(2R) -methoxycarbonyl-(4R) - (methylsulfonoxy) pyrrolidine
204072-65-1P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
azidopyrrolidine 204072-66-2P, N-(4-Butoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-aminopyrrolidine 204072-67-3P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
propylaminopyrrolidine 204072-68-4P, N-(4-Methoxyphenylsulfonyl)-
(2R) -methoxycarbonyl - (4S) -n-hexylaminopyrrolidine 204072-69-5P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-
phenylethylamino)pyrrolidine 204072-70-8P, N-(4-
Methoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4S) - (N-butyl-N-
hexylamino)pyrrolidine 204072-71-9P 204072-72-0P,
N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
[(methanesulfonyl)amino]pyrrolidine 204072-74-2P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(3-
pyridylmethyl)amino]pyrrolidine 204072-75-3P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-(3-pyridylmethyl)-
N-(methanesulfonyl)amino]pyrrolidine 204072-76-4P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N,N-
bis (methanesulfonyl) amino] pyrrolidine 204072-77-5P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-
(methanesulfonyl) propylamino] pyrrolidine 204072-78-6P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(4-
methoxyphenylsulfonyl) amino]pyrrolidine 204072-79-7P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-
oxohexyl) aminopyrrolidine 204072-81-1P 204072-82-2P,
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RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (intermediate; preparation of substituted cyclic amines as metalloprotease inhibitors for treating conditions characterized by excess activity of these enzymes)
RN 204072-54-8 HCAPLUS
CN D-Proline, 4-hydroxy-1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)
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57850-07-4P, N-(4-Methylphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
IT
    hydroxypyrrolidine 203934-42-3P, N-(4-Methoxyphenylsulfonyl)-
     (2R) -methoxycarbonyl-4-oxopyrrolidine 203934-63-8P
     203994-80-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
     (4R) -hydroxypyrrolidine 203994-82-5P, N-(4-
     Methoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4S) -acetylthiopyrrolidine
     204072-15-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
     (4S)-benzoyloxypyrrolidine 204072-16-2P, N-(4-
    Methoxyphenylsulfonyl) - (2S) -methoxycarbonyl - (4R) -hydroxypyrrolidine
     204072-17-3P, N-(4-Methoxyphenylsulfonyl)-(2S)-methoxycarbonyl-
     (4S)-hydroxypyrrolidine 204072-19-5P, N-(4-
     Methoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4S) -methoxypyrrolidine
     204072-20-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
     (4R) - (trifluoromethanesulfonyloxy)pyrrolidine 204072-21-9P
     204072-23-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
     (4R) - [(benzothiazol-2-yl)thio]pyrrolidine 204072-24-2P,
     N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-methyl-2-
     imidazolylthio]pyrrolidine 204072-25-3P, N-(4-
     Methoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4R) - [N-methyl-2-
     imidazolylthio]pyrrolidine 204072-26-4P, N-(4-
     Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-phenoxypyrrolidine
     204072-27-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
     (4S) - (4-benzyloxyphenoxy) pyrrolidine 204072-28-6P,
     N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-
     phenylaminophenoxy) pyrrolidine 204072-29-7P,
     N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-
     pyridinyloxy)pyrrolidine 204072-30-0P, N-(4-
     Methoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4S) -phenylthiopyrrolidine
     204072-31-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-
     (4R) - (methanesulfonyloxy) pyrrolidine 204072-32-2P,
     N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(4-
     methoxyphenylthio) pyrrolidine 204072-34-4P, N-(4-
     Methoxyphenylsulfonyl) - (2R) -methoxycarbonyl - (4S) - (3-
     methoxyphenylthio)pyrrolidine 204072-36-6P, N-(4-
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US 2002072517	A1	20020613	US	2001-888759		20010625 <
US 2003191163	A 1	20031009	US	2002-308780		20021203 <
US 6858628	B2	20050222				
JP 2004115531	A2	20040415	JP	2003-384116		20031113
US 2004138260	A1	20040715	US	2003-730572		20031208
US 2005101567	A1	20050512	US	2004-3594		20041203
PRIORITY APPLN. INFO.:			US	1996-24842P	P	19960828
			US	1997-918317	A2	19970826
			US	2001-888675	A2	20010625
			US	2001-888759	A2	20010625
			JP	1998-511715	A3	19970822
			US	2002-186531	A2	20020701
			US	2002-308780	A3	20021203

OTHER SOURCE(S):

GI

MARPAT 139:22213

Ι

$$\begin{array}{c|c}
 & O_2S \\
 & N \\
 &$$

The invention provides compds. having a structure according to formula (I) AΒ [wherein A = each (un) substituted alkyl, heteroalkyl, aryl, heteroaryl; R1 = NHOR2 (where R2 = hydrogen or alkyl); W = H, lower alkyl, or an alkylene bridge that forms a ring in addition to the ring depicted in the formula; Y = HO, SR3, SOR4, SO2R8, alkoxy, (un) substituted NH2; R4 = alkyl, aryl, heteroaryl; R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino; Z = H, HO, alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the ring depicted in the formula; n = 1; provisos given] or pharmaceutically acceptable salts, or biohydrolyzable amides, esters, or imides thereof. These compds. are useful as inhibitors of metalloproteases, in particular zinc metalloprotease, and effective in treating conditions characterized by excess activity of these enzymes, e.g. degenerative diseases such as arthritis and multiple sclerosis and inflammation (no data). Thus, cis-Hydroxy-D-proline (50 g, 0.38 mol) was dissolved in water:dioxane (1:1, 300 mL) with Et3N (135 mL, 0.96 mol), treated with 4-Methoxyphenylsulfonyl chloride (87 g, 0.42 mol) along with 2,6-dimethylaminopyridine (4.6 g, 0.038 mol), stirred for 14 h at room temperature, concentrated, and diluted with EtOAc to give, after workup, N-(4-Methoxyphenylsulfonyl)-(4R)-hydroxypyrrolidine-(2R)-carboxylic acid. This intermediate was dissolved in MeOH (500 mL), treated dropwise with 50 mL SOC12, stirred for 14 h, evaporated, to dryness, and triturated with CHCl3 to give N-4-Methoxyphenylsulfonyl-(2R)-carbomethoxy-(4R)hydroxypyrrolidine as a white solid which was sufficiently pure to carry forward without purification The latter Me ester (361 mg, 1.15 mmol) was taken in 1 mL MeOH, treated with NH2OK (1.45 mL, 0.86 M in methanol), and stirred overnight to give, after workup, N-4-Methoxyphenylsulfonyl-(2R)-Nhydroxycarboxamido-(4S)-hydroxypyrrolidine.

204072-54-8P, N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-IT methoxycarbonyl-(4R)-hydroxypyrrolidine

Ward 10 663042

EP 2002-796635 20021214 20040929 EP 1461022 A2 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK JP 2003-552279 T2 20050512 20021214 JP 2005513060 EP 2001-129951 20011217 PRIORITY APPLN. INFO.: EP 2002-9555 20020426 Δ EP 2002-23936 Α 20021025 WO 2002-EP14279 W 20021214

The invention discloses the use of PDE5 inhibitors for the treatment of AB patients having a pulmonary disorder in which in which a pulmonary ventilation-pulmonary perfusion mismatch is present.

259191-82-7 IT

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase 5 inhibitors for treatment of pulmonary disease with ventilation-perfusion mismatch)

259191-82-7 HCAPLUS RN

4-Piperidinecarboxylic acid, 1-[[3-[[4,7-dihydro-3-(1-methyl-4-CN phenylbutyl) -7-oxo-3H-1,2,3-triazolo[4,5-d]pyrimidin-5yl]methyl]phenyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

L32 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:435318 HCAPLUS

DOCUMENT NUMBER:

139:22213

TITLE:

Preparation of substituted cyclic amines as

metalloprotease inhibitors

INVENTOR(S):

Natchus, Michael George; De, Biswanath; Pikul, Stanislaw; Almstead, Neil Gregory; Bookland, Roger

Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S):

The Procter & Gamble Company, USA

SOURCE:

U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S.

Ser. No. 888,675.

CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

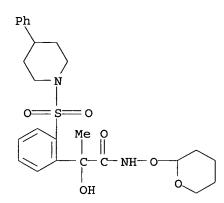
PATENT INFORMATION:

PATENT NO. KI		DATE	APPLICATION NO.	DATE			
US 2003105153	A1	20030605	US 2002-186531	20020701 <			
US 6872742	B2	20050329	o				
US 6417219	B1	20020709	US 1997-918317	19970826 <			
US 2002061877	A1	20020523	US 2001-888675	20010625 <			
US 6569855	B2	20030527					

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)

RN 308386-08-5 HCAPLUS

CN Benzeneacetamide, α-hydroxy-α-methyl-2-[(4-phenyl-1 piperidinyl)sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX
 NAME)



REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:491029 HCAPLUS

DOCUMENT NUMBER:

139:63337

TITLE:

Use of selective phosphodiesterase 5 (PDE5) inhibitors

in the treatment of pulmonary diseases having a

ventilation-perfusion mismatch

INVENTOR (S):

Ghofrani, Ardeschir; Grimminger, Friedrich Josef;

Schudt, Christian

PATENT ASSIGNEE(S):

Altana Pharma AG, Germany

SOURCE:

PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND D	DATE AF	DATE	
WO 2003051346	A2 2	20030626 WC	20021214 <	
WO 2003051346	A3 2	20040212		
W: AE, AL,	AU, BA, BR,	CA, CN, CO, C	CU, DZ, EC, GE, H	R, HU, ID, IL,
IN, IS,	JP, KR, LT,	LV, MA, MK, M	IX, NO, NZ, PH, P	L, RO, SG, TN,
UA, US,	VN, YU, ZA,	ZW		
RW: AM, AZ,	BY, KG, KZ,	MD, RU, TJ, T	CM, AT, BE, BG, C	H, CY, CZ, DE,
DK, EE,	ES, FI, FR,	GB, GR, IE, I	T, LU, MC, NL, P	T, SE, SI, SK, TR

RN 308385-92-4 HCAPLUS

CN Benzamide, 2-[(4-phenyl-1-piperidinyl)sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

RN 308386-04-1 HCAPLUS

CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 308386-05-2 HCAPLUS

CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} Ph & O \\ & \parallel \\ & \parallel \\ O & CO_2H \end{array}$$

RN 308386-06-3 HCAPLUS

IT 213012-83-0P 213012-84-1P 213012-85-2P

308385-92-4P 308386-04-1P 308386-05-2P

308386-06-3P 308386-08-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as matrix metalloprotease inhibitors)

RN 213012-83-0 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 213012-84-1 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 213012-85-2 HCAPLUS

CN Benzamide, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

Ward 10 663042

effective amount to a host having a condition associated with pathol. MMP activity. Thus, thioetherification of 4-phenoxybenzenethiol with 2-fluorobenzaldehyde in the presence of K2CO3 in isopropanol under reflux for 20 h gave 2-(4-phenoxyphenylthio)benzaldehyde which was condensed with tetra-Et dimethylaminomethylenediphosphonate in the presence of NaH in THF at room temperature for 4 h gave to 2-[2-(4-phenoxyphenylthio)phenyl]acetic

(II). II was oxidized by H2O2 in acetic acid to 2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetic acid which was condensed with O-tetrahydropyranylhydroxylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in MeCN followed by treatment with p-toluenesulfonic acid in methanol at room temperature for 2 h

give N-hydroxy-2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetamide (III). III and N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide showed IC50 of >10,000 nM against MMP-1, 0.3 and 2.4 nM, resp., against MMP-2, and 2 and 2.7 nM, resp., against MMP-13.

IT 213012-59-0P, N-Hydroxy-2-[[4-(phenylmethyl)-1piperidinyl]sulfonyl]benzamide 308385-44-6P,
N-Hydroxy-2-[[4-(phenyl)-1-piperidinyl]sulfonyl]benzamide
308385-45-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as matrix metalloprotease inhibitors)

RN 213012-59-0 HCAPLUS

acid

to

CN Benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{Ph-CH}_2 & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & &$$

RN 308385-45-7 HCAPLUS

CN Benzeneacetamide, N,α-dihydroxy-α-methyl-2-[(4-phenyl-1piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)

PA	PATENT NO.							APPLICATION NO.						DATE					
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				20040921									100000104						
WC									WO 1998-US4300 CN, CU, CZ, EE, GE, GH,										
		W:																	
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			PL.	RO,	SG,	SI,	SK,	SL,	TR,	TT,	UA,	US,	UΖ,	VN,	ΥU,	AM,	ΑZ,	BY,	
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OTHER SOURCE(S):

MARPAT 139:307685

Ι

The title compds. [I; m, n = 0 or 1 and the sum of m + n is 0 or 1; the AB ring structure W is a 5- or 6-membered aromatic or heteroarom. ring; X = CH2 or (un) substituted NH2; R1 = (i) a substituent containing a 5- or 6-membered cyclohydrocarbyl, heterocyclyl, aryl or heteroaryl radical bonded directly to the depicted SO2 group or (ii) (un)substituted; R2, R3 = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, O- or S-(un)substituted hydroxyalkyl or mercaptoalkyl, hydroxy, thiol, haloalkyl, N-(un)substituted amino, aminoalkyl, aminoalkanoylaminoalkyl, aminoalkoxy, or aminoalkoxyalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylthio, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylthio; or CR2R3 together forms an (un) substituted 4- to 8-membered carbocyclic or heterocyclic ring, that is preferably a 5- or 6-membered ring; R5, R6 = H, alkyl, cycloalkyl, acylalkyl, halo, NO2, HO, cyano, alkoxy, haloalkyl, haloalkoxy, hydroxyalkyl, N-(un)substituted aminoalkyl or aminoalkoxy, thiol, alkylthio, arylthio, cycloalkylthio, cycloalkoxy, alkoxyalkoxy, perfluoroalkyl, haloalkyl, heterocyclyloxy; or R5 and R6 together with the atoms to which they are bonded form a further aliphatic or aromatic carbocyclic or heterocyclic ring having 5- to 7-members; R20 = each (un) substituted OH, NHOH, or NH2] or pharmaceutically acceptable salts thereof are prepared Also disclosed is a treatment process that comprises administering a contemplated sulfonyl aromatic or heteroarom. ring hydroxamic acid compound in a matrix metalloprotease (MMP) enzyme-inhibiting

204072-11-7 HCAPLUS

CN2-Pyrrolidinecarboxamide, N-hydroxy-4-(3-methyl-2,5-dioxo-1imidazolidinyl) -1-[(4-phenoxyphenyl) sulfonyl] -, (2R,4S) - (9CI) (CA INDEX

Absolute stereochemistry.

L32 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:796371 HCAPLUS

DOCUMENT NUMBER: 139:307685

Preparation of sulfonyl aryl or heteroaryl hydroxamic TITLE:

acid compounds as matrix metalloprotease inhibitors Bedell, Louis J.; Mcdonald, Joseph J.; Barta, Thomas

INVENTOR (S): E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos,

John N.; Mischke, Brent V.; Getman, Daniel P.;

Decrescenzo, Gary A.; Villamil, Clara I.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S. Pat. Appl. Publ., 200 pp., Cont.-in-part of U.S.

Ser. No. 230,209.

CODEN: USXXCO Patent

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: 10

PATENT INFORMATION:

RN 204072-09-3 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-[(4S)-4-methyl-2,5-dioxo-1-imidazolidinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-10-6 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204072-07-1 HCAPLUS

CN· 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,5-dioxo-3-(2-propenyl)-1-imidazolidinyl]-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-08-2 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204072-05-9 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-06-0 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204072-03-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-04-8 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204072-01-5 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-02-6 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

204071-99-8 HCAPLUS RN

2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

204072-00-4 HCAPLUS RN

2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204071-59-0 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 4-ethyl-N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204071-60-3 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204071-62-5 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, (2R,4R)- (9CI) (CA INDEX NAME)

(preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as
 metalloprotease inhibitors for treatment of restenosis)
RN 204072-55-9 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4R) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

204071-58-9P 204071-59-0P, 1-(4-Methoxyphenylsulfonyl)тт (2R) - (N-hydroxycarboxamido) - (4R) -4-hydroxy-4-ethylpyrrolidine 204071-60-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) - (4R) -4-hydroxy-4-phenylpyrrolidine 204071-62-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) -3,3-dimethyl-(4R)-hydroxypyrrolidine 204071-99-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) - (4S) - (1-piperidyl)pyrrolidine 204072-00-4P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1piperidyl)pyrrolidine 204072-01-5P, 1-(4-Methoxyphenylsulfonyl)-(2R) - (N-hydroxycarboxamido) - (4S) - (morpholino) pyrrolidine 204072-02-6P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) - (4S) - (morpholino) pyrrolidine 204072-03-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1dioxothiomorpholino) pyrrolidine 204072-04-8P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1dioxothiomorpholino)pyrrolidine 204072-05-9P 204072-06-0P 204072-07-1P 204072-08-2P 204072-09-3P 204072-10-6P 204072-11-7P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as metalloprotease inhibitors for treatment of restenosis) 204071-58-9 HCAPLUS RN2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-CN , (2R,3S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 722550-49-4 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(2-methoxyethyl)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 722550-52-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 204072-55-9P, 1-(4-Phenoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[[(2,3-dihydro-3-methyl-1H-imidazol-1-yl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-35-1 HCAPLUS

CN D-Proline, 4-([1,1'-biphenyl]-4-ylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 722550-48-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(methylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 204073-04-1 HCAPLUS

CN D-Proline, 4,4-bis(ethylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-28-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-32-8 HCAPLUS

RN 204072-99-1 HCAPLUS

CN D-Proline, 1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204073-00-7 HCAPLUS

CN D-Proline, 4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-97-9 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-98-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(4S)-4-methyl-2,5-dioxo-1-imidazolidinyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

204072-95-7 HCAPLUS RN

D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

RN

204072-96-8 HCAPLUS D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,5-dioxo-3-(2-propenyl)-1-imidazolidinyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME) CN

RN 204072-93-5 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1,1-dioxido-4-thiomorpholinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-94-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-91-3 HCAPLUS
CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, methyl ester,
(4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-92-4 HCAPLUS
CN D-Proline, 4-(1,1-dioxido-4-thiomorpholinyl)-1-[(4-methoxyphenyl)sulfonyl], methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-89-9 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-90-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-87-7 HCAPLUS

CN D-Proline, 4-[[(2R)-2-hydroxy-1-oxo-3-phenylpropyl]propylamino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-88-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-85-5 HCAPLUS

CN D-Proline, 4-[[(2R)-2-hydroxy-1-oxopropyl]propylamino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-86-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-3-phenyl-2-(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-82-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-83-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-3-phenyl-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-84-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-2-(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

RN 204072-79-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-oxohexyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-81-1 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(methylamino)carbonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-77-5 HCAPLUS
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)propylamino]-,
 methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-78-6 HCAPLUS
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(4-methoxyphenyl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-74-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-75-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-76-4 HCAPLUS

CN D-Proline, 4-[bis(methylsulfonyl)amino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-71-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-72-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(methylsulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-68-4 HCAPLUS

CN D-Proline, 4-(hexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-69-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(2-phenylethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-70-8 HCAPLUS

CN D-Proline, 4-(butylhexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Ward 10_663042

RN 204072-65-1 HCAPLUS

CN D-Proline, 4-azido-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-66-2 HCAPLUS

CN D-Proline, 4-amino-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-67-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(propylamino)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 204072-60-6 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-61-7 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-62-8 HCAPLUS

CN D-Proline, 4-azido-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-

RN 204072-57-1 HCAPLUS

CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-58-2 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-59-3 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN204072-52-6 HCAPLUS

D-Proline, 1-[(2,4-dichlorophenyl)sulfonyl]-4-hydroxy-, methyl ester, CN(4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN204072-56-0 HCAPLUS

D-Proline, 4-hydroxy-1-[[4-(2-methylpropoxy)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 204072-47-9 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-50-4 HCAPLUS

CN D-Proline, 1-[(4-bromophenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-51-5 HCAPLUS

CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-hydroxy-, methyl ester,

Ward 10_663042

RN 204072-44-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-45-7 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-46-8 HCAPLUS

CN D-Proline, 1-[(3,4-dimethoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-, methyl ester, (3S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 204072-41-3 HCAPLUS
CN D-Proline, 4-ethyl-4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,

(CA INDEX NAME)

Absolute stereochemistry.

(4R)- (9CI)

RN 204072-42-4 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, methyl
 ester, (4R)- (9CI) (CA INDEX NAME)

CN D-Proline, 4-(ethoxymethoxy)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-37-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(phenylmethoxy)methoxy]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-38-8 HCAPLUS

CN D-Proline, 4-[(2-methoxyethoxy)methoxy]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-39-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(phenylthio)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-32-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-34-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-36-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(phenylmethoxy)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-28-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(phenylamino)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-29-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-30-0 HCAPLUS

RN 204072-25-3 HCAPLUS
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-yl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 204072-27-5 HCAPLUS

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-23-1 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-24-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-yl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-20-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-21-9 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-22-0 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-

Absolute stereochemistry.

RN 204072-17-3 HCAPLUS
CN L-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-19-5 HCAPLUS CN D-Proline, 4-methoxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

Ward 10_663042

722550-49-4P, 1-[4-(2-Methoxyethyl)phenylsulfonyl]-(2R)carbomethoxy-(4R)-hydroxypyrrolidine 722550-52-9P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-5-pyrrolidinone
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
 (intermediate; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid
 as metalloprotease inhibitors for treatment of restenosis)
RN 57850-07-4 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-methylphenyl)sulfonyl]-, methyl ester, (4R)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 203934-42-3 HCAPLUS CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 203934-63-8 HCAPLUS CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

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methylsulfonyloxypyrrolidine 204072-65-1P, 1-(4-
Butoxyphenylsulfonyl) - (2R) -carbomethoxy- (4S) -azidopyrrolidine
204072-66-2P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
aminopyrrolidine 204072-67-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carbomethoxy-(4S)-propylaminopyrrolidine 204072-68-4P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(hexylamino)pyrrolidine
204072-69-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
(2-phenylethylamino)pyrrolidine 204072-70-8P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(N-butyl-N-
hexylamino)pyrrolidine 204072-71-9P, 1-(4-Methoxyphenylsulfonyl)-
(2R) -carbomethoxy-(4S) - [(methanesulfonyl)amino]pyrrolidine
204072-72-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
[(methanesulfonyl)amino]pyrrolidine 204072-74-2P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(3-
pyridylmethyl)amino)pyrrolidine 204072-75-3P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(3-pyridylmethyl)-N-
(methanesulfonyl)amino]pyrrolidine 204072-76-4P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
[bis (methanesulfonyl) amino] pyrrolidine 204072-77-5P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(methanesulfonyl)-N-
propylamino)pyrrolidine 204072-78-6P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy- (4S) - [(4-
methoxyphenylsulfonyl)amino]pyrrolidine 204072-79-7P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
(hexanoylamino)pyrrolidine 204072-81-1P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy-(4S) -
[(methylcarbamoyl)amino]pyrrolidine 204072-82-2P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-
benzyloxypropyl)amino]pyrrolidine 204072-83-3P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-
benzyloxy-3-phenylpropyl)amino]pyrrolidine 204072-84-4P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-
benzyloxypropyl) -N-propylamino]pyrrolidine 204072-85-5P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-
hydroxypropyl) -N-propylamino]pyrrolidine 204072-86-6P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-
benzyloxy-3-phenylpropyl)-N-propylamino]pyrrolidine 204072-87-7P
 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-
hydroxy-3-phenylpropyl)-N-propylamino]pyrrolidine 204072-88-8P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1-
piperidyl)pyrrolidine 204072-89-9P, 1-(4-Butoxyphenylsulfonyl)-
(2R) -carbomethoxy-(4S)-(1-piperidyl)pyrrolidine 204072-90-2P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(morpholino)pyrrolidine
204072-91-3P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
(morpholino)pyrrolidine 204072-92-4P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy- (4S) - (1,1-
dioxothiomorpholino)pyrrolidine 204072-93-5P,
1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1,1-
dioxothiomorpholino)pyrrolidine 204072-94-6P
204072-95-7P 204072-96-8P 204072-97-9P
204072-98-0P 204072-99-1P 204073-00-7P
204073-04-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-4,4-
bis (ethylthio) pyrrolidine 537704-28-2P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy-(4S) - [4-(1,1,3,3-
tetramethylbutyl)phenoxy]pyrrolidine 537704-32-8P,
1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[[(1-methyl-3-
imidazolyl)sulfonyl]amino]pyrrolidine 537704-35-1P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-
biphenylylamino)pyrrolidine 722550-48-3P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy-(4R) - (methanesulfonyl) pyrrolidine
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204072-16-2P, 1-(4-Methoxyphenylsulfonyl)-(2S)-carbomethoxy-(4R)-
hydroxypyrrolidine 204072-17-3P, 1-(4-Methoxyphenylsulfonyl)-
(2S) -carbomethoxy-(4S) -hydroxypyrrolidine 204072-19-5P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-methoxypyrrolidine
204072-20-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-
[(trifluoromethanesulfonyl)oxy]pyrrolidine 204072-21-9P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-
benzothiazolylthio)pyrrolidine 204072-22-0P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-hydroxypyrrolidine
204072-23-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-
(2-benzothiazolylthio)pyrrolidine 204072-24-2P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1-methyl-2-
imidazolylthio)pyrrolidine 204072-25-3P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy- (4R) - (1-methyl-2-imidazolylthio)pyrrolidine 204072-26-4P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy-(4S) -phenoxypyrrolidine
204072-27-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
[4-(benzyloxy)phenoxy]pyrrolidine 204072-28-6P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-
phenylaminophenoxy)pyrrolidine 204072-29-7P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-
pyridinyloxy)pyrrolidine 204072-30-0P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy-(4S) -phenylthiopyrrolidine
204072-32-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
(4-methoxyphenylthio)pyrrolidine 204072-34-4P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-
methoxyphenylthio)pyrrolidine 204072-36-6P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy-(4R) -ethoxymethoxypyrrolidine
204072-37-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-
benzyloxymethoxypyrrolidine 204072-38-8P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy-(4R) - [(2-
methoxyethoxy) methoxy] pyrrolidine 204072-39-9P
204072-41-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-4-
hydroxy-4-ethylpyrrolidine 204072-42-4P, 1-(4-
Methoxyphenylsulfonyl) - (2R) -carbomethoxy- (4R) -4-hydroxy-4-
phenylpyrrolidine 204072-44-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carbomethoxy-3,3-dimethyl-4-oxopyrrolidine 204072-45-7P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-3,3-dimethyl-(4R)-
hydroxypyrrolidine 204072-46-8P, 1-(3,4-Dimethoxyphenylsulfonyl)-
(2R) -carbomethoxy-(4R) -hydroxypyrrolidine 204072-47-9P,
1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-
hydroxypyrrolidine 204072-50-4P, 1-(4-Bromobenzenesulfonyl)-(2R)-
carbomethoxy-(4R)-hydroxypyrrolidine 204072-51-5P,
1-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-carbomethoxy-(4R)-
hydroxypyrrolidine 204072-52-6P, 1-(2,4-Dichlorophenylsulfonyl)-
(2R) -carbomethoxy-(4R) -hydroxypyrrolidine 204072-56-0P,
1-(4-Isobutyloxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine
204072-57-1P, 1-(2-Methyl-4-bromophenylsulfonyl)-(2R)-carbomethoxy-
(4S) - (3-methoxyphenylthio) pyrrolidine 204072-58-2P,
1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-
benzothiazolylthio)pyrrolidine 204072-59-3P,
1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-
benzothiazolylthio)pyrrolidine 204072-60-6P,
1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-
methoxyphenylthio)pyrrolidine 204072-61-7P, 1-(4-
Butoxyphenylsulfonyl) - (2R) -carbomethoxy-(4S) - (3-pyridyloxy)pyrrolidine
204072-62-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-
azidopyrrolidine 204072-63-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-
carbomethoxy-(4S)-aminopyrrolidine 204072-64-0P,
1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-
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OTHER SOURCE(S):

MARPAT 141:123901

GI

AΒ The invention provides compds. according to formula (I), in particular N-sulfonylpyrrolidine-2-carbohydroxamic acid derivs., [wherein A = each (un) substituted alkyl, heteroalkyl, aryl, or heteroaryl; R1 = NHOR2 (where R2 = H, alkyl); W = one or more of H, lower alkyl, or an alkylene bridge that forms a ring in addition to the main ring; Y = independently one or more of HO, SR3, SOR4, SO2R8, alkoxy, or (un) substituted amino (where R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino); Z = H, HO, or alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the main ring; n = 1; some provisos applied], pharmaceutically-acceptable salts, biohydrolyzable amides, esters, or imides thereof are prepared These compds. are useful as inhibitors of metalloproteases, and effective in treating conditions characterized by excess activity of these enzymes, in particular restenosis. Thus, cis-hydroxy-D-propine was condensed with 4-methylphenylsulfonyl chloride in the presence of Et3N and 2,6-dimethylpyridine in aqueous dioxane at room temperature for 14 h gave N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine which was esterified with MeOH and SOCl2 to give N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine Me ester which was treated with hydroxylamine monopotassium salt in MeOH overnight to give (2R,4S)-1-(4-Methoxyphenylsulfonyl)-2-(Nhydroxycarboxamido) -4S-hydroxypyrrolidine.

IT 57850-07-4P, 1-(4-Methylphenylsulfonyl)-(2R)-carbomethoxy-(4R)hydroxypyrrolidine 203934-42-3P, 1-(4-Methoxyphenylsulfonyl)(2R)-carbomethoxy-4-oxopyrrolidine 203934-63-8P,
1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine
203994-80-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)hydroxypyrrolidine 203994-82-5P, 1-(4-Methoxyphenylsulfonyl)(2R)-carbomethoxy-(4S)-acetylthiopyrrolidine 204072-15-1P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-benzoyloxypyrrolidine

Ward 10 663042

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2002-380761P P 20020514 PRIORITY APPLN. INFO.: US 2002-392782P Р 20020628 US 2002-422933P р 20021031 US 2002-428033P P 20021120 WO 2003-US15343 A2 20030514

OTHER SOURCE(S): MARPAT 141:218994

AB Administering an ED of a tTGase inhibitor to a celiac sprue or dermatitis herpetiformis patient reduces the toxic effects of toxic gluten oligopeptides, thereby attenuating or eliminating the damaging effects of gluten. Preparation and tissue transglutaminase-inhibiting activity of dihydroisoxazole moiety-containing compds. is included.

IT 220509-86-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tissue transglutaminase inhibitor therapy for celiac sprue and dermatitis herpetiformis)

RN 220509-86-4 HCAPLUS

CN L-Proline, 1-[(2,3-dihydro-2,3-dioxo-1H-indol-5-yl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L32 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:569862 HCAPLUS

DOCUMENT NUMBER:

141:123901

TITLE:

Preparation of N-sulfonyl-cyclic amine-2-

carbohydroxamic acid derivatives as metalloprotease

inhibitors

INVENTOR(S):

Natchus, Michael George; De, Biswanath; Pikul, Stanislaw; Almstead, Neil Gregory; Bookland, Roger Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S.

Ser. No. 186,531.

CODEN: USXXCO

DOCUMENT TYPE:

Patent English

LANGUAGE:

- Endit

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138260	A1	20040715	US 2003-730572	20031208
US 6417219	B1	20020709	US 1997-918317	19970826 <
US 2002061877	A1	20020523	US 2001-888675	20010625 <
US 6569855	B2	20030527		

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L32 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:703116 HCAPLUS

DOCUMENT NUMBER: 141:218994

TITLE: Tissue transglutaminase (tTGase) inhibitor therapy for

celiac sprue and dermatitis herpetiformis

INVENTOR(S): Khosla, Chaitan; Choi, Kihang

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of Appl.

No. PCT/US03/15343.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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							IN,											
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							IN,							-				
							MD,											
		PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	
		TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW						
	RW:	GH,	GM,	KΕ,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	ΤZ,	ŪĠ,	ZM,	ZW,	AM,	ΑZ,	BY,	
		KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	ВG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	
		FI,	FR,	GB,	GR,	HU,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,	
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
EP	1507	549			A2		20050223			EP 2003-728939			20030514					
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
							RO,											
WO	20040			-	A2		2004			WO 2				•		0031	120	
WO	WO 2004045392			A 3		20040826												
	W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR.	BW.	BY.	BZ.	CA.	CH.	
							DE,						-			-	-	
							ID,		-	_	-	-	-	-	-	-	-	
							LV,											
							PT,						-		-	-	-	
							UA,									ZW	10,	
	рw.						MW,										Δσ	
	TCM :						TJ,											
		DI,	κσ,	NΔ,	, עויו	κυ,	ΙU,	I 1"1,	мı,	DE,	ъG,	Cn,	CI,	CZ,	υĽ,	DΚ,	cc,	

Ward 10_663042

VAR G1=1/4/9/14/29 REP G2=(1-5) C NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

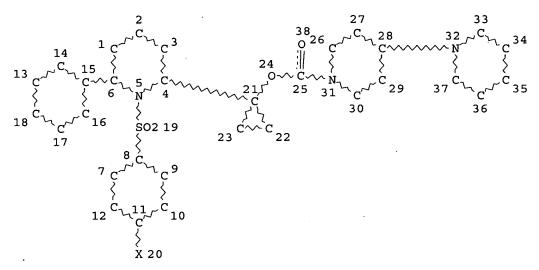
RSPEC I

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10

L13 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

=>

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

L15	5	SEA	FILE=REGISTRY	Y SUB=L12	2 SSS FUI	L L13
L16	3	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L15
L17	25432	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L12 NOT L15
L18	183	SEA	FILE=REGISTRY	Y ABB=ON	PLU=ON	SECRETASE
L19	3443	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L17
L20	2011	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L18 OR ?SECRETASE?
L21	9	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L19 AND L20
L22	6	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L21 NOT L16
L23	450	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L19(L)INHIBIT?
L24	372	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L23 AND PD= <december 2003<="" 8,="" td=""></december>
L25	301	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L24 AND PATENT/DT
L29	78	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L23 AND ENZYME(L)INHIBIT?
L31	35	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L29 AND L25
L32	35	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L31 NOT (L16 OR L22)

Page 30

Absolute stereochemistry.

REFERENCE COUNT:

16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> 🗆

=> d stat que

L4

STR

Ak \(^C \) \(\) \

Ak~O~Ak

G1\sim Hy\sim SO2Cy 16 15 8 9

@12 13 14 16 15 8

VAR G1=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/10/12

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

GGCAT IS MCY AT 15

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE L10 STR

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@9

8 c C 10

8 c 10

12 N C

Cy SO2

24 23

AB A novel methodol. utilizing the aza-Payne rearrangement and O, N-intramol. acyl transfer reactions for the synthesis of peptidomimetics containing hydroxyethylamine dipeptide isosteres (HDIs) (e.g., I) is described. This methodol. is useful for the stereoselective synthesis of HDI-containing pseudopeptides, and applicable to combinatorial chemical using solid-phase techniques.

IT 433922-90-8P 433922-91-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of hydroxyethylamine dipeptide isostere-containing peptidomimetics

as potential β - secretase inhibitors using aza-Payne rearrangement)

RN 433922-90-8 HCAPLUS

CN Aziridine, 2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-(2-methylpropyl)-1-[(2,4,6-trimethylphenyl)sulfonyl]-, (2S,3R)- (9CI) (CAINDEX NAME)

Absolute stereochemistry.

RN 433922-91-9 HCAPLUS

CN Aziridine, 2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-(2-methylpropyl)-1-[(2,4,6-trimethylphenyl)sulfonyl]-, (2S,3S)- (9CI) (CFINDEX NAME)

Ward 10 663042

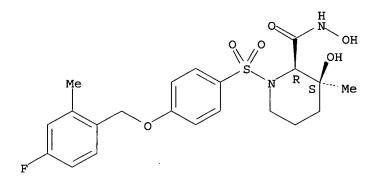
(Biological study); USES (Uses)

(TACE and metalloprotease inhibitor CP-661,631 prevents amyloid precursor protein secretion but does not increase amyloid β levels)

530135-92-3 HCAPLUS RN

2-Piperidinecarboxamide, 1-[[4-[(4-fluoro-2-methylphenyl)methoxy]phenyl]su CN lfonyl]-N,3-dihydroxy-3-methyl-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:288617 HCAPLUS

DOCUMENT NUMBER: 137:20588

TITLE: Efficient stereoselective synthesis of peptidomimetics

containing hydroxyethylamine dipeptide isosteres utilizing the aza-Payne rearrangement and O, N-acyl

transfer reactions

Tamamura, Hirokazu; Hori, Tadakazu; Otaka, Akira; AUTHOR (S):

Fujii, Nobutaka

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto

University, Kyoto, 606-8501, Japan

SOURCE: Journal of the Chemical Society, Perkin Transactions 1

(2002), (5), 577-580 CODEN: JCSPCE; ISSN: 1472-7781 Royal Society of Chemistry

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:20588

GI

PUBLISHER:

L22 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:3568 HCAPLUS

DOCUMENT NUMBER: 138:396061

TITLE: Effect of tumor necrosis factor- α converting

enzyme (TACE) and metalloprotease inhibitor on amyloid

precursor protein metabolism in human neurons Blacker, Megan; Noe, Mark C.; Carty, Thomas J.;

AUTHOR(S): Blacker, Megan; Noe, Mark C.; Carty, Thomas

Goodyer, Cynthia G.; LeBlanc, Andrea C.

CORPORATE SOURCE: The Bloomfield Center for Research in Aging, Lady

Davis Institute for Medical Research, Montreal, QC,

Can:

SOURCE: Journal of Neurochemistry (2002), 83(6), 1349-1357

CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

Tumor necrosis factor- α (TNF- α) is implicated in inflammatory processes and much effort is being directed at inhibiting the release of $TNF-\alpha$ for treatment of inflammatory conditions. In this context, the drug CP-661,631 has been developed to inhibit the TNF- α converting enzyme (TACE). However, TACE is also implicated in amyloid precursor protein secretion. Amyloid precursor protein (APP) undergoes constitutive and regulated secretion by $\alpha\text{-}$ secretaseendoproteolytic cleavage within the amyloid β peptide (Aβ) domain. Alternative cleavage at the N- and C-terminus of the $A\beta$ domain by β - and γ - secretases results in the production of AB. In many cellular and in vivo animal models, increased secretion of APP results in a concomitant decrease in the production of Aß suggesting that the two pathways are intricately linked. However, in human primary neuron cultures, increased APP secretion is not associated with a decrease in total $A\beta$ production To determine if the use of CP-661,631 may enhance amyloidogenic processing in human brain, we have assessed the effect of CP-661,631 on APP metabolism in primary cultures of human neurons. Our results show that CP-661,631 effectively prevents regulated APP secretion but does not increase total AB levels in human primary neuron cultures.

IT **530135-92-3**, CP 661631

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

RN 527728-27-4 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-4-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 527728-83-2 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-3-[[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]carbonyl]-5-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 527726-39-2 HCAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 527728-13-8 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-3-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c|c} & \text{Me} & & \text{OH} & \\ & & \text{H} & & \text{H} \\ & & \text{O} & & \\ & & & \text{N} & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\$$

The title compds. [I; R1 = (un) substituted alkyl, alkenyl, alkynyl, etc.; AB R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un) substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un)substituted CH2; R6 = (un) substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β - secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5difluorophenyl)propanoic acid, was given. The compds. I showed IC50 of < 20 μM in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 158736-49-3, β - Secretase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating
Alzheimer's disease)

II

RN 158736-49-3 HCAPLUS

CN β -Secretase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 527716-81-0P 527726-39-2P 527728-13-8P 527728-27-4P 527728-83-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 527716-81-0 HCAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[(2S)-2-(methoxymethyl)1-pyrrolidinyl]sulfonyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Ward 10 663042

Company

SOURCE:

PCT Int. Appl., 1243 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

DATE APPLICATION NO. PATENT NO. KIND DATE ------------------------WO 2002-US36072 20021108 WO 2003040096 A2 20030515 WO 2003040096 A3 20040506 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, NA. UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AZ 20030515 WO 2002-XA36072 20021108

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OTHER SOURCE(S):

MARPAT 138:385173

US 2002-345635P WO 2002-US36072

RN 597560-81-1 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-3-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]carbonyl]-5-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L22 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:376819 HCAPLUS

DOCUMENT NUMBER: 138:385173

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-

hydroxypropanes for treating Alzheimer's disease INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang,

Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John;

Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 527728-13-8 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-3-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 527728-27-4 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-4-[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Ward 10 663042

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.: US 2001-337122P Ρ 20011108 US 2001-344086P Ρ 20011228 US 2002-345635P Р 20020103 WO 2002-US36072 20021108 OTHER SOURCE(S): MARPAT 139:245782

OTHER SOURCE(S):

GΙ

$$\operatorname{Pr}_{2}\mathbb{N}$$
 OH $\operatorname{H}_{\mathbb{N}}$ OMe

The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; AΒ R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un) substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un) substituted CH2; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β - secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5difluorophenyl)propanoic acid, was given. The compds. I showed IC50 of < 20 μM in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.

IT 527726-39-2P 527728-13-8P 527728-27-4P 597560-81-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

ΙI

527726-39-2 HCAPLUS

RN

INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:412801 HCAPLUS

DOCUMENT NUMBER:

139:245782

TITLE:

Preparation of N,N'-substituted-1,3-diamino-2hydroxypropanes for treating Alzheimer's disease Varghese, John; Maillard, Michel; Jagodzinska,

INVENTOR(S):

Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John;

Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S):

Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn

Company

SOURCE:

PCT Int. Appl., 1243 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

		APPLICATION NO.	
WO 2002040006	72 20020515		
		WO 2002-XA36072	
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY, F	3Z, CA, CH, CN,
CO, CR, CU,	CZ, DE, DK, DM,	DZ, EC, EE, ES, FI, G	B, GD, GE, GH,
GM, HR, HU,	ID, IL, IN, IS,	JP, KE, KG, KP, KR, K	KZ, LC, LK, LR,
LS, LT, LU,	LV, MA, MD, MG,	MK, MN, MW, MX, MZ, N	NO, NZ, OM, PH,
PL, PT, RO,	RU, SD, SE, SG,	SI, SK, SL, TJ, TM, T	rn, TR, TT, TZ,
UA, UG, US,	UZ, VN, YU, ZA,	ZM, ZW, AM, AZ, BY, K	KG, KZ, MD, RU,
TJ, TM			
RW: GH, GM, KE,	LS, MW, MZ, SD,	SL, SZ, TZ, UG, ZM, Z	ZW, AT, BE, BG,
CH, CY, CZ,	DE, DK, EE, ES,	FI, FR, GB, GR, IE, I	IT, LU, MC, NL,
PT, SE, SK,	TR, BF, BJ, CF,	CG, CI, CM, GA, GN, G	GQ, GW, ML, MR,
NE, SN, TD,	TG		
WO 2003040096	A2 20030515	WO 2002-US36072	20021108
WO 2003040096	A3 20040506		
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY, B	3Z, CA, CH, CN,
• • • • • • • • • • • • • • • • • • • •		DZ, EC, EE, ES, FI, G	• •
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• • • •		MK, MN, MW, MX, MZ, N	
		SI, SK, SL, TJ, TM, T	
12, 11, 10,	,,,	,,, 10, 111, 1	,,,

Relative stereochemistry.

L22 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:534852 HCAPLUS

DOCUMENT NUMBER: 140:77384

TITLE: Synthesis of potent β - secretase

inhibitors containing a hydroxyethylamine dipeptide isostere and their structure-activity relationship

studies

AUTHOR(S): Tamamura, Hirokazu; Kato, Terukazu; Otaka, Akira;

Fujii, Nobutaka

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto

University, Sakyo-ku, Kyoto, 606-8501, Japan

SOURCE: Organic & Biomolecular Chemistry (2003), 1(14),

2468-2473

CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:77384

AB Several β - secretase inhibitors were designed based on hydroxyethylamine dipeptide isostere (HDI) structures and were synthesized by a methodol. using the aza-Payne rearrangement and O,N-acyl transfer reactions to study their structure-activity relationships. Amongst these pseudopeptides, effective compds. were developed as the first β - secretase inhibitors containing the HDI transition state mimic with

potent enzyme inhibitory activity (IC50 < 100 nM).

IT 158736-49-3, β - Secretase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of hydroxyethylamine dipeptide isostere-based pseudopeptides as

potent β - secretase inhibitors and their structure-activity relationship studies)

RN 158736-49-3 HCAPLUS

CN β-Secretase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 433922-91-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of hydroxyethylamine dipeptide isostere-based pseudopeptides using aza-Payne rearrangement reaction of a protected aziridine)

RN 433922-91-9 HCAPLUS

CN Aziridine, 2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-(2-methylpropyl)-1-[(2,4,6-trimethylphenyl)sulfonyl]-, (2S,3S)- (9CI) (CA

Ward 10 663042

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PATENT NO.
                                 KIND
                                          DATE
                                                           APPLICATION NO.
                                                                                          DATE
                                 _ _ _ _
                                                            -----
      US 2004229902
                                  A1
                                           20041118
                                                           US 2004-842783
                                                                                          20040511
                                                           WO 2004-US14671
      WO 2004101562
                                  A2
                                           20041125
                                                                                          20040511
      WO 2004101562
                                  A3
                                           20050210
                 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
                 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
           RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                                           US 2003-470146P
OTHER SOURCE(S):
                                 MARPAT 141:424116
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

- AB The invention relates to a preparation of bridged N-(arylsulfonyl)piperidine derivs. of formula I [wherein: Ar is (hetero)aryl; X is O, NH, NH, or N-aryl, etc.; Y is (CH2)0-3-R7; Z is (CH2)0-3; R1 is 1 to 3 independent substituents selected from H, alkyl, CN, NO2, NH2, etc.; R2 is H, (cyclo)alkyl, alkylene-O-alkyl, or (hetero)aryl, etc.; R3 is 1 to 6 independent substituents H, halogen, (cyclo) alkyl, or OCF3, etc.; R4 and R7 are independently selected from H, alkyl, or aryl; R4 and R7 together with the ring carbon atoms may form a cycloalkyl ring; R5 is (cyclo)alkyl, NH2, NH-alkyl, (hetero)aryl, or NH-(hetero)aryl, etc.; R6 is H, (hetero)aryl, (cyclo)alkyl, or -alkylene-heteroaryl, etc.], useful as γ - secretase inhibitors. The prepared compds. are useful for the treatment of Alzheimer's disease. For instance, N-(arylsulfonyl)piperidine derivative II (IC50 is within the range of about 0.1 to about 1.0 µM) was prepared via Ru-catalyzed intramol. cyclization of bis(alkenyl)piperidine derivative III, hydrogenation of the obtained azabicyclo[3.3.1]nonene derivative IV, O-carboxylation, and amidation by N-(2-hydroxyethyl)piperazine.
- IT 338454-52-7, γ Secretase
 - RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; preparation of bridged N-(arylsulfonyl)piperidine derivs. useful as γ secretase inhibitors)
- RN 338454-52-7 HCAPLUS
- CN γ -Secretase (9CI) (CA INDEX NAME)
- *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
- IT 796042-81-4P
 - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 - (preparation of bridged N-(arylsulfonyl)piperidine derivs. useful as γ secretase inhibitors)
- RN 796042-81-4 HCAPLUS
- CN 2-Piperidinecarboxylic acid, 1-[(4-chlorophenyl)sulfonyl]-6-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-, methyl ester, (2R,6S)-rel- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L4
                STR
L10
                STR
L12
          25437 SEA FILE=REGISTRY SSS FUL L4 AND L10
L13
                STR
L15
              5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13
L16
              3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15
L17
          25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15
L18
            183 SEA FILE=REGISTRY ABB=ON
                                          PLU=ON SECRETASE
L19
           3443 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON L17
L20
           2011 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                 L18 OR ?SECRETASE?
L21
              9 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                 L19 AND L20
L22
              6 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                 L21 NOT L16
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=> d ibib abs hitstr 122 1-6

L22 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:999679 HCAPLUS

DOCUMENT NUMBER: 141:424116

TITLE: A preparation of bridged N-(arylsulfonyl)piperidine

derivatives, useful as γ - secretase

inhibitors

INVENTOR(S): Josien, Hubert B.

PATENT ASSIGNEE(S): Schering Corporation, USA SOURCE: U.S. Pat. Appl. Publ., 37 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

RN 579499-99-3 HCAPLUS CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-

chlorophenyl)sulfonyl]-6-(2,4-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 579500-00-8 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-; 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 579499-92-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)

RN 579499-96-0 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME) GI

$$(R^3)_2$$

$$R^{11}$$

$$(R^3)_2$$

$$(R^3)_0$$

$$(R^3)_1$$

$$(R^3)_2$$

$$(R^3)_2$$

$$(R^3)_2$$

$$(R^3)_2$$

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$$(R^3)_1$$

$$(R^3)_2$$

$$(R^3)_1$$

$$(R^3)_1$$

$$(R^3)_2$$

$$(R^3)_1$$

$$(R^3)$$

AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloclkylene-alkylene-XCOY, or (un) substitute (hetero) aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un) substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as γ -secretase inhibitors, which inhibit the deposition of β-amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K2CO3. The aldehyde was converted to the alc. with NaBH4 and protected with t-BuPh2SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited γ-secretase activity in transfected human APP cells with an IC50 value in the range of about 0.0002 μM to about 15 μM. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

IT 579499-91-5P 579499-92-6P 579499-96-0P 579499-99-3P 579500-00-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

 $(\gamma$ -secretase inhibitor; preparation of 1-(arylsulfonyl)piperidines as γ -secretase inhibitors for treatment of neurodegenerative diseases)

RN 579499-91-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L16 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:633663 HCAPLUS

DOCUMENT NUMBER: 139:179979

TITLE: Preparation of 1-(arylsulfonyl)piperidines as

 γ -secretase inhibitors for treatment of

neurodegenerative diseases

INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,

Elizabeth M.; Clader, John W.; Asberom, Theodros; Guo,

Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia, Inc.

SOURCE: PCT Int. Appl., 170 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE .		
WO 2003066592	A1 200308	14 WO 2003-US3471	20030205		
W: AE, AG, A	, AM, AT, AU, A	Z, BA, BB, BG, BR, BY,	BZ, CA, CH, CN,		
CO, CR, C	Z, DE, DK, DM, D	Z, EC, EE, ES, FI, GB,	GD, GE, HR, HU,		
ID, IL, I	I, IS, JP, KG, K	R, KZ, LC, LK, LR, LT,	LU, LV, MA, MD,		
MG, MK, M	I, MX, MZ, NO, N	Z, PH, PL, PT, RO, RU,	SC, SE, SG, SK,		
SL, TJ, T	1, TN, TR, TT, T	Z, UA, UZ, VC, VN, YU,	ZA, ZM		
RW: GH, GM, K	E, LS, MW, MZ, S	D, SL, SZ, TZ, UG, ZM,	ZW, AM, AZ, BY,		
KG, KZ, M	O, RU, TJ, TM, A	T, BE, BG, CH, CY, CZ,	DE, DK, EE, ES,		
FI, FR, G	B, GR, HU, IE, I	T, LU, MC, NL, PT, SE,	SI, SK, TR, BF,		
BJ, CF, C	G, CI, CM, GA, G	N, GQ, GW, ML, MR, NE,	SN, TD, TG		
CA 2478423	AA 200308	14 CA 2003-2478423	20030205		
EP 1472223	A1 200411	03 EP 2003-737650	20030205		
R: AT, BE, C	H, DE, DK, ES, F	R, GB, GR, IT, LI, LU,	NL, SE, MC, PT,		
IE, SI, L	r, LV, FI, RO, M	K, CY, AL, TR, BG, CZ,	EE, HU, SK		
BR 2003007492	A 200411	23 BR 2003-7492	20030205		
PRIORITY APPLN. INFO.:		US 2002-355618P	P 20020206		
		WO 2003-US3471	W 20030205		
OTHER SOURCE(S):	MARPAT 139:17	9979			

THER SOURCE(S): MARPAT 139:179979

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)

RN 579499-99-3 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(2,4-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Relative stereochemistry.

 $\gamma\text{-secretase}$ inhibitors for treatment of neurodegenerative diseases)

RN 579499-91-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 579499-92-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)

RN 579499-96-0 HCAPLUS

US 2003-663042

A 20030916

OTHER SOURCE(S):

MARPAT 141:207066

$$R^{3}$$
 R^{11}
 R^{2}
 R^{2}
 R^{3}
 R^{3}
 R^{2}
 R^{3}
 R^{3}
 R^{2}
 R^{3}
 $R^{$

ΙI

Title compds. I [wherein R1 = (un) substituted (hetero) aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un) substituted (hetero) aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un) substituted (hetero) aryl, alkyl, (hetero) cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero) aryl, alkyl, (hetero) cycloalkyl, etc.; m = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as γ -secretase inhibitors, which inhibit the deposition of β-amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K2CO3. The aldehyde was converted to the alc. with NaBH4 and protected with t-BuPh2SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited γ -secretase activity in transfected human APP cells with an IC50 value in the range of about 0.0002 μM to about 15 μM. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

IT 579499-91-5P 579499-92-6P 579499-96-0P

579499-99-3P 579500-00-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(y-secretase inhibitor; preparation of (arylsulfonyl)piperidines as

L16 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:722916 HCAPLUS

DOCUMENT NUMBER: 141:207066

TITLE: Preparation of 1-(arylsulfonyl)piperidines as

 γ -secretase inhibitors for treatment of

neurodegenerative diseases

INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,

Elizabeth M.; Clader, John W.; Asberom, Theodros; Guo,

Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S): Schering-Plough Corporation, USA; Pharmacopeia, Inc.

SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S.

Ser. No. 358,898.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT	NO.		KINI) I	DATE		i	APPL:	ICAT:	ION 1	. OI		Dž	ATE	
US 2004	171614		A1	•	2004	0902		US 2	002-	5620	 12		2.	0030	216
				_	2004	0902	,	05 2	003-	2020.	± 4		۷ ر	0030	910
US 2004	048848		A1	2	2004	0311	I	US 2	003-3	3588	98		20	0030:	205
WO 2005	028440		A1	- 2	2005	0331	1	WO 2	004-1	JS30:	191		20	0040	915
W:	AE, A	G, AL,	AM,	AΤ,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
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	GE, G	H, GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,
	LK, L	R, LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
	NO, N	Z, OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
	TJ, Ť	M, TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ΥU,	ZA,	ZM,	ZW
RW:	BW, G	H, GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	AM,
	AZ, B	Y, KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
	EE, E	S, FI,	FR,	GB,	GR,	HU,	ΙE,	ΙT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
	SI, S	K, TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,
	SN, T	D, TG													
US 2005	085506		A1	2	2005	0421	1	US 2	004-	94144	40		20	0040	915
PRIORITY APPLN. INFO.: US 2002-355618P P 20020206							206								
							1	US 2	003-3	3588	98	1	A2 20	00302	205

RN 579499-99-3 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(2,4-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 579500-00-8 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-,
1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl
ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 579499-92-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)

RN 579499-96-0 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)

AΒ Title compds. I [wherein R1 = (un) substituted (hetero) aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un) substituted (hetero) aryl, etc.; R3 = H, alkyl, OH, alkoxy, etc.; R3a, R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un) substituted amino, hydrazino, (hetero) aryl, alkyl, (hetero) cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as γ-secretase inhibitors, which inhibit the deposition of β -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K2CO3. The aldehyde was converted to the alc. with NaBH4 and protected with t-BuPh2SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchlorocarbonate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited γ -secretase activity in transfected human APP cells with an IC50 value in the range of about $0.0002~\mu\text{M}$ to about 15 μM . Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

II

IT INDEXING IN PROGRESS

IT 579499-91-5P 579499-92-6P 579499-96-0P 579499-99-3P 579500-00-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

 $(\gamma$ -secretase inhibitor; preparation of (arylsulfonyl)piperidines as γ -secretase inhibitors for treatment of neurodegenerative diseases)

RN 579499-91-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-

Ward 10 663042

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

L15 5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13 L16 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15

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=> d ibib abs hitstr l16 1-3

L16 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:346733 HCAPLUS

TITLE: Preparation of 1-(arylsulfonyl)piperidines as

γ-secretase inhibitors for treatment of

neurodegenerative diseases

INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,

Elizabeth M.; Clader, John W.; Asberom, Theodros; Guo,

Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S): Schering-Plough Corp., USA; Pharmacopeia, Inc.

SOURCE: U.S. Pat. Appl. Publ., 170 pp., Cont.-in-part of U.S.

Ser. No. 663,042.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005085506	A1	20050421	US 2004-941440	20040915
US 2004048848	A1	20040311	US 2003-358898	20030205
US 2004171614	A 1	20040902	US 2003-663042	20030916
PRIORITY APPLN. INFO.:			US 2002-355618P P	20020206
			US 2003-358898 A	2 20030205
			US 2003-663042 A	2 20030916

GI

VAR G1=1/4/9/14/29 REP G2=(1-5) C NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10 L13 STR

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

Ward 10 663042

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FILE COVERS 1907 - 13 May 2005 VOL 142 ISS 21 FILE LAST UPDATED: 12 May 2005 (20050512/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d stat que

L4 STR

Ak Cy Ak O Ak G1 Hy SO2Cy @10 11 @12 13 14 16 15 8 9

VAR G1=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/10/12 NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM GGCAT IS MCY AT 15 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RSPEC I

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE L10 STR

RN 204072-52-6 HCAPLUS

CN D-Proline, 1-[(2,4-dichlorophenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-55-9 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-56-0 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(2-methylpropoxy)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-57-1 HCAPLUS

CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-58-2 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-59-3 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-60-6 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-61-7 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-62-8 HCAPLUS CN D-Proline, 4-azido-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 204072-65-1 HCAPLUS CN D-Proline, 4-azido-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME) Absolute stereochemistry.

RN 204072-66-2 HCAPLUS

CN D-Proline, 4-amino-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-67-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(propylamino)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-68-4 HCAPLUS

CN D-Proline, 4-(hexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,

Absolute stereochemistry.

RN 204072-69-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(2-phenylethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-70-8 HCAPLUS

CN D-Proline, 4-(butylhexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-71-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-72-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(methylsulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-74-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-75-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-76-4 HCAPLUS

CN D-Proline, 4-[bis(methylsulfonyl)amino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-77-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-78-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(4-methoxyphenyl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-79-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-oxohexyl)amino]-, methyl ester, (4S)- (9CI). (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-81-1 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(methylamino)carbonyl]amino], methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-82-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-83-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-3-phenyl-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-84-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-2-(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

204072-85-5 HCAPLUS RNCN

D-Proline, 4-[[(2R)-2-hydroxy-1-oxopropyl]propylamino]-1-[(4methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

204072-86-6 HCAPLUS RN

D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[(2R)-1-oxo-3-phenyl-2-CN(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-87-7 HCAPLUS

CN D-Proline, 4-[[(2R)-2-hydroxy-1-oxo-3-phenylpropyl]propylamino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-88-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-89-9 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-90-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-92-4 HCAPLUS
CN D-Proline, 4-(1,1-dioxido-4-thiomorpholinyl)-1-[(4-methoxyphenyl)sulfonyl], methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-93-5 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1,1-dioxido-4-thiomorpholinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204073-01-8 HCAPLUS

CN Proline, 1-[(4-methoxyphenyl)sulfonyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 537704-28-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-31-7 HCAPLUS

CN D-Proline, 4-amino-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-, monoformate (9CI) (CA INDEX NAME)

CM 1

CRN 204072-63-9 CMF C13 H18 N2 O5 S

CM 2

CRN 64-18-6 CMF C H2 O2

О=== СН− ОН

RN 537704-32-8 HCAPLUS
CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[[(2,3-dihydro-3-methyl-1H-imidazol-1-yl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-35-1 HCAPLUS
CN D-Proline, 4-([1,1'-biphenyl]-4-ylamino)-1-[(4-methoxyphenyl)sulfonyl]-,
methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 537704-63-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-66-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

J

537704-68-0 HCAPLUS RN

D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,4-dioxo-3-(2-propenyl)-1-imidazolidinyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

537704-72-6 HCAPLUS RN

D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(5,5-dimethyl-2,4-dioxo-1-CNimidazolidinyl) -, methyl ester, (4S) - (9CI) (CA INDEX NAME)

537704-74-8 HCAPLUS RN

D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(5S)-5-methyl-2,4-dioxo-1-CN imidazolidinyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

537704-76-0 HCAPLUS D-Proline, 1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,4-dioxo-1-CNimidazolidinyl) -, methyl ester, (4S) - (9CI) (CA INDEX NAME)

RN 537704-78-2 HCAPLUS
CN D-Proline, 4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

204071-58-9P 204071-59-0P, N-(4-Methoxyphenylsulfonyl)-IT (2R) - (N-hydroxycarboxamido) - (4R) -4-hydroxy-4-ethylpyrrolidine 204071-60-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) - (4R) -4-hydroxy-4-phenylpyrrolidine 204071-62-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) -3,3-dimethyl-(4R)-hydroxypyrrolidine 204071-99-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) - (4S) - (1-piperidyl)pyrrolidine 204072-00-4P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1piperidyl)pyrrolidine 204072-01-5P, N-(4-Methoxyphenylsulfonyl)-(2R) - (N-hydroxycarboxamido) - (4S) -morpholinopyrrolidine 204072-02-6P, N-(4-Butoxyphenylsulfonyl)-(2R)-(Nhydroxycarboxamido) - (4S) -morpholinopyrrolidine 204072-03-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1dioxothiomorpholino) pyrrolidine 204072-04-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1dioxothiomorpholino)pyrrolidine 537704-65-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1methylimidazolidin-3-yl)pyrrolidine 537704-67-9P,

Ward 10_663042

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N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-
    methylimidazolidin-3-yl)pyrrolidine 537704-69-1P,
    N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-
    allylimidazolidin-3-yl)pyrrolidine 537704-73-7P,
    N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,4-dioxo-5,5-
    dimethylimidazolidin-1-yl)pyrrolidine 537704-75-9P,
    N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(5S)-5-methyl-
    2,4-dioxoimidazolidin-1-yl]pyrrolidine 537704-77-1P,
    N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-(N-hydroxycarboxamido)-(4S)-(3-
    methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-79-3P,
    N-(4-Phenoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methyl-2,4-
    dioxoimidazolidin-1-yl)pyrrolidine 537704-80-6P,
    N-(4-Methoxyphenylsulfonyl)-(2R)-hydroxycarboxamido-(4R)-4-hydroxy-4-
    ethylpyrrolidine
    RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (preparation of substituted cyclic amines as metalloprotease
       inhibitors for treating conditions characterized by excess
       activity of these enzymes)
RN
     204071-58-9 HCAPLUS
     2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-
CN
     , (2R,3S)-rel- (9CI)
                          (CA INDEX NAME)
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Relative stereochemistry.

RN 204071-59-0 HCAPLUS
CN 2-Pyrrolidinecarboxamide, 4-ethyl-N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4R)- (9CI) (CA INDEX NAME)

RN 204071-60-3 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204071-62-5 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204071-99-8 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204072-00-4 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-01-5 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204072-02-6 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-03-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 204072-04-8 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-65-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 537704-67-9 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-69-1 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,4-dioxo-3-(2-propenyl)-1-imidazolidinyl]-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 537704-73-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(5,5-dimethyl-2,4-dioxo-1-imidazolidinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-75-9 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-[(5S)-5-methyl-2,4-dioxo-1-imidazolidinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 537704-77-1 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 537704-79-3 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-1-[(4-phenoxyphenyl)sulfonyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

RN 537704-80-6 HCAPLUS

CN 3-Pyrrolidinecarboxamide, 3-ethyl-5-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (3R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L32 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:22851 HCAPLUS

DOCUMENT NUMBER:

138:55878

TITLE:

Preparation of bispiperidines as antibacterial agents

and inhibitors of phosphopantetheine adenylyl

transferase.

INVENTOR(S):

Lampe, Thomas; Ehlert, Kerstin; Freiberg, Christoph;

Schiffer, Guido

PATENT ASSIGNEE(S):

Bayer Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002534	A1	20030109	WO 2002-EP6640	20020617 <
W: AE. AG. AL.	AM. AT	. AU. AZ. BA	. BB. BG. BR. BY. BZ.	CA. CH. CN.

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                GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
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                                                       DE 2001-10138234
                                                                                   20010803
                               MARPAT 138:55878
OTHER SOURCE(S):
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GI

$$R^{1}$$
 SO_{2} R^{3}

AΒ Use of title compds. [I; A = O, (CH2)n; n = 0-2; R1-R3 = H, halo, alkyl, cycloalkyl, alkoxy, alkoxycarbonyl, etc.; or R1R2 = C6 aryl, 5-8 membered heterocyclyl; R3 = H, halo, alkyl, cycloalkyl, alkoxy, alkoxycarbonyl, alkylcarbonyl, amino, etc.; R4 = H, alkyl, cycloalkyl, alkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, etc.], for treatment of bacterial infection is claimed. I are useful for the treatment of diseases caused by bacteria requiring phosphopantetheine adenylyl transferase (CoaD) enzyme for CoA synthesis. Tested I (general preparation given) inhibited CoaD activity with IC50 = 0.65-12.5 μM, and showed min. inhibitory concns. of <0.2 µM to 100 µM against B. subtilis Al 796.

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479620-22-9P 479620-23-0P 479620-24-1P
479620-25-2P 479620-26-3P 479620-27-4P
479620-28-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
   (preparation of bispiperidines as antibacterial agents and
   inhibitors of phosphopantetheine adenylyl transferase)
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RN 219140-19-9 HCAPLUS
CN Piperidine, 1-[(2,5-dimethoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl](9CI) (CA INDEX NAME)

RN 341020-80-2 HCAPLUS
CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-fluorophenyl)sulfonyl]- (9CI)
(CA INDEX NAME)

RN 479618-65-0 HCAPLUS
CN Piperidine, 1-[(2,5-dimethylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl](9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 N S O Me

479618-66-1 HCAPLUS RN

Piperidine, 1-[(3,5-dichloro-4-methylphenyl)sulfonyl]-4-[3-(4-CN piperidinyl)propyl] - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

479618-67-2 HCAPLUS RN

Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(2,5-dimethoxyphenyl)sulfonyl]-CN (9CI) (CA INDEX NAME)

RN

479618-68-3 HCAPLUS
Piperidine, 1-[(4-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-CN (9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 N S 0 Me

RN 479618-69-4 HCAPLUS

Piperidine, 4,4'-(1,2-ethanediyl)bis[1-[(2,5-dimethoxyphenyl)sulfonyl]-CN(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OMe} & \text{OMe} \\ \hline \\ \text{O} & \text{S} \\ \hline \\ \text{OMe} & \text{O} \\ \end{array}$$

RN 479618-70-7 HCAPLUS

CN Piperidine, 1-[(3-chlorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-71-8 HCAPLUS

CN Piperidine, 4-[2-(4-piperidinyl)ethyl]-1-[(2,4,6-trimethylphenyl)sulfonyl]-(9CI) (CA INDEX NAME)

RN 479618-72-9 HCAPLUS

CN Piperidine, 1-[(3-chloro-4-fluorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 479618-73-0 HCAPLUS

CN Piperidine, 1-[(3,5-dichloro-4-methylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 479618-74-1 HCAPLUS

CN Piperidine, 1-[(4-methoxyphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & \\ & & & & \\ \text{HN} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 479618-75-2 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 479618-76-3 HCAPLUS

CN Piperidine, 1-[(4-methyl-3-nitrophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-77-4 HCAPLUS

CN Piperidine, 1-[[2-methyl-5-(trifluoromethyl)phenyl]sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{CH}_2 - \text{CH}_2 & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 479618-78-5 HCAPLUS

CN 4-Morpholinecarboxamide, N-[3-chloro-4-[[4-[2-(4-piperidinyl)ethyl]-1-piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

RN 479618-79-6 HCAPLUS

CN Piperidine, 1-[(4-methylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ \text{CH}_2 - \text{CH}_2 & & \\ & & & \\ \end{array}$$

RN 479618-80-9 HCAPLUS

CN Piperidine, 1-(phenylsulfonyl)-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-81-0 HCAPLUS

CN Piperidine, 1-[(3-methylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-82-1 HCAPLUS

CN Piperidine, 1-[(2-methoxy-4-methylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-83-2 HCAPLUS

CN Piperidine, 1-[(3-fluorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 479618-84-3 HCAPLUS

CN Piperidine, 1-[(3-cyanophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-85-4 HCAPLUS

CN Piperidine, 1-[(2,5-dimethylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \text{HN} & & \\ & & \\ \text{CH}_2\text{--} \text{CH}_2 & \\ & & \\$$

RN 479618-86-5 HCAPLUS

CN Piperidine, 1-[(4-chlorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{CH}_2 - \text{CH}_2 & & & \\ & & & \\ \end{array}$$

RN 479618-87-6 HCAPLUS

CN Piperidine, 1-[(2,6-difluorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl](9CI) (CA INDEX NAME)

RN 479618-88-7 HCAPLUS

CN Piperidine, 1-[(5-fluoro-2-methoxyphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-89-8 HCAPLUS

CN Piperidine, 4-[2-(4-piperidinyl)ethyl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ & & & \\ & &$$

RN 479618-90-1 HCAPLUS

CN Piperidine, 1-[(2,6-dichlorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]-(9CI) (CA INDEX NAME)

RN 479618-91-2 HCAPLUS

CN Piperidine, 1-[(1-formyl-2,3-dihydro-1H-indol-5-yl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 479618-92-3 HCAPLUS

CN Acetamide, N-[3-methyl-4-[[4-[2-(4-piperidinyl)ethyl]-1-piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ \text{CH}_2 - \text{CH}_2 \end{array} \begin{array}{c} & & \\ & &$$

RN 479618-93-4 HCAPLUS

CN Piperidine, 1-[(2,5-dimethoxyphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl](9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{OMe} \\ & \\ \text{O} \\ & \\ \text{CH}_2-\text{CH}_2 \\ & \\ \text{O} \\ & \\ \text{OMe} \\ \end{array}$$

RN 479618-94-5 HCAPLUS

CN Piperidine, 4,4'-(1,2-ethanediyl)bis[1-[(2-methoxy-4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479618-95-6 HCAPLUS
CN Piperidine, 4,4'-(1,2-ethanediyl)bis[1-[(5-fluoro-2-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479618-96-7 HCAPLUS

CN Piperidine, 1-[(3-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-(9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 $N = S$ Me

RN 479618-97-8 HCAPLUS

CN Piperidine, 1-[(3-cyanophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 N S CN

RN 479618-98-9 HCAPLUS

CN Piperidine, 1-{(4-chlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-(9CI) (CA INDEX NAME)

Ward 10 663042

479618-99-0 HCAPLUS RN

Piperidine, 1-[(3-chlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-CN (CA INDEX NAME)

HN
$$C1$$
 $CH_2)_3$ O $C1$

479619-00-6 HCAPLUS RN

Piperidine, 4-[3-(4-piperidinyl)propyl]-1-[(2,4,6-CN trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

479619-01-7 HCAPLUS
Piperidine, 1-[(3-chloro-4-fluorophenyl)sulfonyl]-4-[3-(4-CN piperidinyl)propyl] - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

479619-02-8 HCAPLUS RN

Piperidine, 1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-[3-(4-CNpiperidinyl)propyl] - (9CI) (CA INDEX NAME)

RN479619-03-9 HCAPLUS

Acetamide, N-[4-[[4-[3-(4-piperidinyl)propyl]-1-CN piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

RN 479619-04-0 HCAPLUS

CN Piperidine, 1-[(4-methyl-3-nitrophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 NO_2 NO_2 Me

RN 479619-05-1 HCAPLUS

CN Piperidine, 4-[3-(4-piperidinyl)propyl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 479619-06-2 HCAPLUS

CN Piperidine, 1-[(2,6-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 N S $C1$ O $C1$

RN 479619-07-3 HCAPLUS

CN Piperidine, 1-[(1-formyl-2,3-dihydro-1H-indol-5-yl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 N S CHO

RN 479619-08-4 HCAPLUS

CN Acetamide, N-[3-methyl-4-[[4-[3-(4-piperidinyl)propyl]-1-piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

RN 479619-09-5 HCAPLUS

CN Piperidine, 1-[[2-methyl-5-(trifluoromethyl)phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{HN} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 479619-10-8 HCAPLUS

CN Piperidine, 1-[[4-[[(dimethylamino)carbonyl]amino]phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\$$

RN 479619-11-9 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl](9CI) (CA INDEX NAME)

RN 479619-12-0 HCAPLUS

CN Piperidine, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-(9CI) (CA INDEX NAME)

RN 479619-13-1 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & &$$

RN 479619-14-2 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479619-15-3 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(3-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479619-16-4 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
C1 & & & \\
O & & & \\
S & N & & \\
O & & & \\
\end{array}$$

$$\begin{array}{c}
C1 \\
N & S \\
O & \\
\end{array}$$

RN 479619-17-5 HCAPLUS

CN Acetamide, N,N'-[1,3-propanediylbis(4,1-piperidinediylsulfonyl-4,1-

phenylene)]bis- (9CI) (CA INDEX NAME)

RN 479619-18-6 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-methyl-3-nitrophenyl)sulfonyl]-(9CI) (CA INDEX NAME)

RN 479619-19-7 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[[2-(trifluoromethyl)phenyl]sulfon yl]- (9CI) (CA INDEX NAME)

RN 479619-20-0 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(2,6-dichlorophenyl)sulfonyl]-(9CI) (CA INDEX NAME)

RN 479619-21-1 HCAPLUS

CN Acetamide, N,N'-[1,3-propanediylbis[4,1-piperidinediylsulfonyl(3-methyl-4,1-phenylene)]]bis- (9CI) (CA INDEX NAME)

RN479619-22-2 HCAPLUS Piperidine, 4,4'-(1,3-propanediyl)bis[1-[[2-methyl-5-CN (trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{CF3} & \text{CCF3} \\ \hline \\ S & N \\ \hline \\ Me & O \end{array}$$

RN

479619-23-3 HCAPLUS
Piperidine, 4,4'-(1,3-propanediyl)bis[1-[[4-[[(dimethylamino)carbonyl]amin CN o]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

PAGE 1-B

- $\mathtt{NMe_2}$

RN 479619-24-4 HCAPLUS

CN 4-Morpholinecarboxamide, N,N'-[1,3-propanediylbis(4,1piperidinediylsulfonyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 479619-25-5 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479619-26-6 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479619-27-7 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479619-29-9 HCAPLUS

CN Piperidine, 1-[(5-chloro-2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CRN 479619-28-8 CMF C20 H31 Cl N2 O2 S

HN
$$(CH_2)_3$$
 N S Me

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-31-3 HCAPLUS

CN Piperidine, 1-[(3-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-30-2 CMF C20 H32 N2 O3 S

HN
$$(CH_2)_3$$
 N S OMe

CM 2

CRN 76-05-1 CMF C2 H F3 O2

479619-33-5 HCAPLUS RN

Piperidine, 1-[(3,4-dimethoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-CN , mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM

CRN 479619-32-4 C21 H34 N2 O4 S CMF

HN
$$(CH_2)_3$$
 $N = S$ 0 0 0 0 0 0

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN

479619-35-7 HCAPLUS
Piperidine, 1-[(2-methoxy-4-methylphenyl)sulfonyl]-4-[3-(4-CNpiperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-34-6 C21 H34 N2 O3 S CMF

76-05-1 CRN CMF C2 H F3 O2

RN

479619-37-9 HCAPLUS
Piperidine, 1-[(4-cyanophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, CNmono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-36-8 CMF C20 H29 N3 O2 S

CM

CRN 76-05-1 CMF C2 H F3 O2

RN479619-39-1 HCAPLUS

Piperidine, 1-[(2,4-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, CNmono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM

CRN 479619-38-0

CMF C19 H28 Cl2 N2 O2 S

HN
$$C1$$
 $C1$
 $C1$
 $C1$
 $C1$
 $C1$
 $C1$

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-41-5 HCAPLUS

CN Piperidine, 1-[[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-40-4

CMF C20 H28 Cl F3 N2 O2 S

HN
$$(CH_2)_3$$
 N S CF_3 O CI

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-43-7 HCAPLUS

CN Acetamide, N-[2-chloro-4-[[4-[3-(4-piperidinyl)propyl]-1-piperidinyl]sulfonyl]phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX

NAME)

CM 1

CRN 479619-42-6

CMF C21 H32 C1 N3 O3 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-45-9 HCAPLUS

CN Piperidine, 4-[3-(4-piperidinyl)propyl]-1-(8-quinolinylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-44-8 CMF C22 H31 N3 O2 S

CRN 76-05-1 CMF C2 H F3 O2

RN

479619-47-1 HCAPLUS
Piperidine, 1-(1-naphthalenylsulfonyl)-4-[3-(4-piperidinyl)propyl]-,
mono(trifluoroacetate) (9CI) (CA INDEX NAME) CN

CM 1

CRN 479619-46-0 CMF C23 H32 N2 O2 S

CM2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-49-3 HCAPLUS

Ward 10_663042

CN Piperidine, 1-[[4-(1-methylethyl)phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-48-2 CMF C22 H36 N2 O2 S

HN
$$(CH_2)_3$$
 N S 0 $Pr-i$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-51-7 HCAPLUS

CN Piperidine, 1-[(2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-50-6 CMF C20 H32 N2 O2 S

HN
$$(CH_2)_3$$
 N S 0 Me

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN

479619-53-9 HCAPLUS
Piperidine, 1-[(2-aminophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, CNmono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM

CRN 479619-52-8 CMF C19 H31 N3 O2 S

HN
$$(CH_2)_3$$
 $N = \begin{bmatrix} 0 \\ | \\ | \\ 0 \end{bmatrix}$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN

479619-54-0 HCAPLUS
Piperidine, 1-[(4-methyl-3-nitrophenyl)sulfonyl]-4-[3-(4-CNpiperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-04-0 CMF C20 H31 N3 O4 S

HN
$$(CH_2)_3$$
 $N = \begin{bmatrix} 0 & NO_2 \\ N & S \\ 0 & 0 \end{bmatrix}$ Me

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-57-3 HCAPLUS

CN Piperidine, 1-[(2-methyl-5-nitrophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-56-2 CMF C20 H31 N3 O4 S

HN
$$(CH_2)_3$$
 $N = S$ Me

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-60-8 HCAPLUS

CN Piperidine, 1-[(2-chlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-59-5

CMF C19 H29 Cl N2 O2 S

HN
$$(CH_2)_3$$
 N S $C1$

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-63-1 HCAPLUS

CN Piperidine, 1-[(2,4-difluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-62-0

CMF C19 H28 F2 N2 O2 S

HN
$$(CH_2)_3$$
 N S S F

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-66-4 HCAPLUS

CN Piperidine, 1-[(2,5-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-65-3 CMF C19 H28 Cl2 N2 O2 S

CM2

76-05-1 CRN C2 H F3 O2 CMF

RN

479619-69-7 HCAPLUS
Piperidine, 1-[(3,5-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, CNmono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-68-6 CMF C19 H28 Cl2 N2 O2 S

HN
$$C1$$
 $C1$ $C1$ $C1$ $C1$ $C1$ $C1$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-71-1 HCAPLUS

CN Piperidine, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-12-0 CMF C20 H32 N2 O3 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-74-4 HCAPLUS

CN Piperidine, 1-[(5-fluoro-2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-73-3 CMF C20 H31 F N2 O2 S

HN (CH₂) 3 N
$$\stackrel{\circ}{\parallel}$$
 $\stackrel{\circ}{\parallel}$ $\stackrel{\circ}{\parallel}$ $\stackrel{\circ}{\parallel}$ $\stackrel{\circ}{\parallel}$ $\stackrel{\circ}{\parallel}$ $\stackrel{\circ}{\parallel}$

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-76-6 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1 '

CRN 479619-11-9 CMF C19 H29 F N2 O2 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-79-9 HCAPLUS

CN Acetamide, N-[4-methoxy-3-[[4-[3-(4-piperidinyl)propyl]-1-piperidinyl]sulfonyl]phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-78-8 CMF C22 H35 N3 O4 S

HN
$$(CH_2)_3$$
 N S O O O O O O

CM .2

CRN 76-05-1 C2 H F3 O2 CMF

RN

479619-82-4 HCAPLUS
Piperidine, 1-[[4-[(aminocarbonyl)amino]phenyl]sulfonyl]-4-[3-(4-CNpiperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM

CRN 479619-81-3 CMF C20 H32 N4 O3 S

$$\begin{array}{c|c} & & & & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & \\ & & \\ & \\ & & \\ & \\ & \\ & & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\$$

CM2

76-05-1 CRN CMF C2 H F3 O2

479619-85-7 HCAPLUS RN

Piperidine, 1-[(2-chloro-4-fluorophenyl)sulfonyl]-4-[3-(4-CN

Ward 10_663042

piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-84-6

CMF C19 H28 Cl F N2 O2 S

HN (CH₂)₃
$$N$$
 S O $C1$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-88-0 HCAPLUS

CN Piperidine, 1-[(2,4-dichloro-5-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-87-9

CMF C20 H30 Cl2 N2 O2 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-90-4 HCAPLUS
CN Acetamide, N-[3-methyl-4-[[4-[3-(4-piperidinyl)propyl]-1piperidinyl]sulfonyl]phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-08-4 CMF C22 H35 N3 O3 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-93-7 HCAPLUS
CN Piperidine, 1-[(4-chloro-2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-92-6 CMF C20 H31 Cl N2 O2 S

HN
$$(CH_2)_3$$
 N S Me

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-96-0 HCAPLUS

CN Piperidine, 1-[(5-chloro-2-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-95-9 CMF C20 H31 Cl N2 O3 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 479619-98-2 HCAPLUS

CN Piperidine, 1-[(3,4-difluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl](9CI) (CA INDEX NAME)

479620-00-3 HCAPLUS RN

Piperidine, 1-[(3,4-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-CN (CA INDEX NAME)

HN
$$C1$$
 $C1$
 $C1$
 $C1$
 $C1$
 $C1$
 $C1$

RN479620-02-5 HCAPLUS

Piperidine, 1-[(3,5-dichloro-2-hydroxyphenyl)sulfonyl]-4-[3-(4-CN piperidinyl)propyl] - (9CI) (CA INDEX NAME)

HN
$$C1$$
 $CH_2)_3$
 $C1$
 $C1$

RN

479620-03-6 HCAPLUS
Piperidine, 1-[(2,4-dimethylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-CN (9CI) (CA INDEX NAME)

479620-04-7 HCAPLUS RN

Piperidine, 1-[(5-acetyl-2-methoxyphenyl)sulfonyl]-4-[3-(4-CNpiperidinyl)propyl] - (9CI) (CA INDEX NAME)

HN
$$(CH_2)_3$$
 N S O O O O O O

479620-05-8 HCAPLUS RN

Piperidine, 1-acetyl-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-CN

piperidinyl]propyl] - (9CI) (CA INDEX NAME)

RN 479620-06-9 HCAPLUS
CN Piperidine, 1-acetyl-4-[3-[1-[(4-methylphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)

RN 479620-08-1 HCAPLUS
CN Piperidine, 4-[3-[1-(4-chlorophenyl)-4-piperidinyl]propyl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 479620-10-5 HCAPLUS
CN Piperidine, 1-[(2,5-dimethoxyphenyl)sulfonyl]-4-[3-[1-[3-(trifluoromethyl)phenyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)

OMe
$$CF_3$$
OMe CF_3

RN 479620-12-7 HCAPLUS
CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-

Ward 10_663042

1-(phenylacetyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & O \\ \hline Ph-CH_2-C & \hline N & \hline \\ O & \hline \\ O & \hline \\ O & \hline \\ O & O \\ \hline \end{array}$$

RN 479620-15-0 HCAPLUS

CN Piperidine, 1-(cyclopropylcarbonyl)-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)

RN 479620-16-1 HCAPLUS

CN Piperidine, 1-benzoyl-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & O \\ \hline O & O \\ \hline Ph-C & O \\ \hline N & S \\ \hline O & O \\ \hline O &$$

RN 479620-17-2 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

OMe
$$CH_2$$
 CH_2 $CH_$

RN 479620-18-3 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-[4-(dimethylamino)benzoyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OMe} & \text{O} & \text{CH}_2 \text{)} \text{ 3} \\ \hline & \text{S} & \text{N} \\ \hline & \text{O} \\ \\ \text{OMe} \end{array}$$

RN 479620-19-4 · HCAPLUS

CN Piperidine, 1-(cyclopropylacetyl)-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)

RN 479620-20-7 HCAPLUS

CN Piperidine, 1-(cyclohexylcarbonyl)-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)

OMe
$$CH_2$$
) 3 N C CH_2) 3 N C

RN 479620-21-8 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-(2-methylbenzoyl)- (9CI) (CA INDEX NAME)

OMe
$$C$$
 CH_2 CH_2

RN 479620-22-9 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)

RN 479620-23-0 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-(methoxyacetyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & O \\ \hline \\ MeO-CH_2-C \\ \hline \\ N & S \\ \hline \\ O & OMe \\ \hline \\ O & OMe$$

RN 479620-24-1 HCAPLUS

CN Piperidine, 1-(2,4-difluorobenzoyl)-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)

OMe
$$CH_2$$
 3 N C F

RN 479620-25-2 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

RN 479620-26-3 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-[(dimethylamino)phenylacetyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} Ph & O \\ | & || \\ Me_2N-CH-C \\ \hline \\ N & S \\ \hline \\ O & OMe \\ \end{array}$$

RN 479620-27-4 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-[3-(1H-imidazol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 479620-28-5 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-[2-(dimethylamino)-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

IT 479618-33-2P 479618-34-3P 479618-35-4P 479618-36-5P 479618-37-6P 479618-38-7P 479618-39-8P 479618-40-1P 479618-41-2P 479618-42-3P 479618-43-4P 479618-44-5P 479618-45-6P 479618-46-7P 479618-47-8P 479618-48-9P 479618-52-5P 479618-53-6P 479618-54-7P 479618-55-8P 479618-56-9P 479618-57-0P 479618-58-1P 479618-59-2P 479618-63-8P 479618-64-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bispiperidines as antibacterial agents and inhibitors of phosphopantetheine adenylyl transferase)

RN 479618-33-2 HCAPLUS CN 1-Piperidinecarboxyl

1-Piperidinecarboxylic acid, 4-[3-[1-[(2,4-dimethylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-34-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(5-acetyl-2-methoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-35-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3-methoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

$$t-BuO-C$$
 N
 $CH_2)_3$
OMe

RN 479618-36-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3,4-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-37-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-methoxy-4-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-38-7 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3-nitrophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-39-8 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-cyanophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-40-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2,4-dichlorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-41-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-42-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-(acetylamino)-3-chlorophenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-43-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-(5-isoquinolinylsulfonyl)-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-44-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[3-[1-(8-quinolinylsulfonyl)-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-45-6 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[3-[1-(1-naphthalenylsulfonyl)-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-46-7 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-(1-methylethyl)phenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-47-8 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-48-9 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-aminophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-49-0 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-methyl-3-nitrophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-50-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-methyl-5-nitrophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-51-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-chlorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-52-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-chloro-6-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-53-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2,5-dichlorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-54-7 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-55-8 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(5-fluoro-2-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-56-9 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-fluorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-57-0 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-[(aminocarbonyl)amino]phenyl]sulf
 onyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX
 NAME)

RN 479618-58-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-chloro-4-fluorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-59-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2,4-dichloro-5-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-60-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-(acetylamino)-2-methylphenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-61-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(5-chloro-2-methoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-62-7 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3-chloro-2-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 479618-63-8 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3,5-dichloro-2-hydroxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

t-BuO-C
$$(CH_2)_3$$
 O OH $C1$

RN 479618-64-9 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[5-(acetylamino)-2-methoxyphenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:754206 HCAPLUS

DOCUMENT NUMBER:

137:273215

TITLE:

Dipeptidyl peptidase inhibitors for the treatment or

prevention of diabetes

INVENTOR (S):

Ashton, Wallace T.; Caldwell, Charles G.; Ok, Hyun;

Parmee, Emma R.; Weber, Ann E.

PATENT ASSIGNEE(S):

Merck & Co., Inc., USA PCT Int. Appl., 94 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.						KIND DATE						DATE							
						-							:		-					
WO	2002	0764	50		A1		2002	1003	1	WO 2	002-1	US89:	31		2	0020	322 <	<		
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,			
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,			
		GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	KΕ,	KG,	KR,	ΚZ,	LC,	LK,	LR,	LS,			
		LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	NZ,	OM,	PH,	PL,			
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,			
		UG,	US,	UΖ,	VN,	ΥU,	ZA,	ZM,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM		
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	BE,	CH,			
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,			
		BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
CA	2441	092			AA		2002	1003		CA 2	002-	2441	092		2	0020	322 <	<		
EP	1385	508			A1		2004	0204		EP 2	002-	7538	19		2	0020	322			
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,			
		ΙE,	SI,	LT,	LV,	FI,	RO,	ΜĶ,	CY,	AL,	TR									
JP	JP 2004525929				T2		2004	0826		JP 2	002-	5749	65	20020322						
US 2004106656					A 1					US 2	003-	4727	71							
PRIORITY	PRIORITY APPLN. INFO.:									US 2	001-	2789	31P	1	P 20010327					
									,	WO 2	002-	US89:	31	٠ ١	W 2	0020	322			
								_			_									

AB The present invention is directed to compds. which are inhibitors of the dipeptidyl peptidase-IV enzyme ("DP-IV inhibitors") and which are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the dipeptidyl peptidase-IV enzyme is involved.

IT 463349-52-2P 463349-54-4P 463349-58-8P

463349-59-9P 463349-71-5P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes)

RN 463349-52-2 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[(4-iodophenyl)sulfonyl]-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 463349-54-4 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-(2-naphthalenylsulfonyl)-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 463349-58-8 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[[4-(1-methylethyl)phenyl]sulfonyl]-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 463349-59-9 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[[4-(trifluoromethoxy)phenyl]sulfonyl]-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

RN463349-71-5 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[(4-iodophenyl)sulfonyl]-3pyrrolidinyl]acetyl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

3

ACCESSION NUMBER:

2002:637683 HCAPLUS

DOCUMENT NUMBER:

137:185504

TITLE:

Preparation of thieno[2,3-d]pyrimidindiones as matrix metalloproteinase inhibitors for treatment of cancer,

rheumatoid arthritis, and osteoarthritis

INVENTOR(S):

Harter, William Glen; Li, Jie Jack; Ortwine, Daniel Fred; Shuler, Kevon Ray; Yue, Wen-song

PATENT ASSIGNEE(S):

SOURCE:

Warner-Lambert Company, USA

PCT Int. Appl., 278 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	rent :	NO.			KIND		DATE			APPL	ICAT	ION 1		DATE					
						-						-		- -	-				
WO	2002	0645	98		A1		2002	0822	1	WO 2	002-	IB20	4		20020118 <				
	W:	ΑE,	AG,	АL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,		
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,		
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,		
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,		
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,		
		UA,	ŪĠ,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,		
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	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AT,	BE,	CH,		
							FR,												
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG		
CA 2433778					AA		2002	0822		CA 2	002-	2433	778	-	2	0020	118 <		

Ward 10_663042

20031217 EP 2002-711123 EP 1370562 **A1** R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR BR 2002007216 Α 20040309 BR 2002-7216 20020118 JP 2002-564529 JP 2004518732 T2 20040624 20020118 US 2003004172 **A**1 20030102 US 2002-75073 20020213 <--PRIORITY APPLN. INFO.: US 2001-268756P Р 20010214 WO 2002-IB204 W 20020118 OTHER SOURCE(S): MARPAT 137:185504 GI

Title fused pyrimidinones I [wherein C2W = 5-membered (hetero)cyclic AB diradical substituted with ABR3 and optionally substituted with R2; A = CO or SO0-2; B = O or NR5; or AB = C.tplbond.C; R1, R4, and R5 = independently H, alkyl, alkenyl, alkynyl, (CH2)n-(hetero)aryl, (CH2)n-cycloalkyl, (CH2)n-heterocyclyl, or alkanoyl; R2 and R3 = independently H, alkyl, alkenyl, alkynyl CN, NO2, NR4R5, (CH2) n-cycloalkyl, or (CH2) n-(hetero) aryl; or R2 = halo; n = 0-5; or NR4R5 = (un)substituted heterocyclyl; with the proviso that R1 and R3 ≠ both H or alkyl; or pharmaceutically acceptable salts thereof] were prepared as matrix metalloproteinase (MMP) inhibitors, especially as selective MMP-13 inhibitors. For example, 3-benzyl-6-chloro-1H-pyrimidine-2.4-dione was coupled with mercaptoacetic acid Et ester using Na2CO3 in EtOH (67%) and the product cyclized with POCl3 in anhydrous DMF to give 3-benzyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidine-6-carboxylic acid Et ester (95%). Saponification (96%) followed by esterification with benzyl

alc. and 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-p-toluenesulfonate afforded II (12%). The latter selectively inhibited the hydrolytic activity of MMP-13 (0.61 $\mu\text{M})$ over MMP-1 (100 $\mu\text{M})$, MMP-2 (100 $\mu\text{M})$, MMP-3 (18 $\mu\text{M})$, MMP-7 (100 $\mu\text{M})$, MMP-9 (100 $\mu\text{M})$, MMP-12 (100 $\mu\text{M})$, and MMP-14 (100 $\mu\text{M})$ with the indicated IC50 values. I are useful for the treatment of diseases mediated by the MMP-13 enzyme, such as cancer, rheumatoid arthritis, or osteoarthritis (no data). Formulations of I are also disclosed.

IT 448965-29-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(MMP inhibitor; preparation of thienopyrimidinediones as MMP inhibitors for treatment of cancer, rheumatoid arthritis, and osteoarthritis)

RN 448965-29-5 HCAPLUS

CN Thieno[2,3-d]pyrimidine-6-carboxamide, 1,2,3,4-tetrahydro-N-[(3-methoxyphenyl)methyl]-1-methyl-3-[[4-[(4-methyl-1-piperidinyl)sulfonyl]phenyl]methyl]-2,4-dioxo-(9CI) (CA INDEX NAME)

IT 448965-30-8

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of thienopyrimidinediones as MMP inhibitors
for treatment of cancer, rheumatoid arthritis, and osteoarthritis)

RN 448965-30-8 HCAPLUS

CN Piperidine, 1-[[4-(bromomethyl)phenyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:449662 HCAPLUS

DOCUMENT NUMBER:

137:33310

TITLE:

Preparation of anilinopyrimidines as IKK inhibitors

INVENTOR(S):

Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka;

Bhagwat, Shripad S.; Parnes, Jason S.; Palanki,

Moorthy S. S.; Erdman, Paul E.

PATENT ASSIGNEE(S):

Signal Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 194 pp.

DOCUMENT TYPE:

CODEN: PIXXD2

DOCUMENT TIP

Patent English

LANGUAGE:

Englis

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.						KIN	D :	DATE		7	APPL	ICAT:		DATE						
	WO	2002	0461	71		A2	-	2002	0613	Ī	WO 2	 001-1	US46	403		20011205 <				
WO 2002046171				A 3		2003	0123													
		W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,		
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,		
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,		
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,		
			DI.	N DT	RO	RII	CD	SE	SG	C T	SK	ST.	T.T	ΤМ	TD	ינוינו	ጥፖ	117		

Ward 10_663042

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UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
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             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                             US 2001-4642
     US 2003203926
                          Α1
                                 20031030
                                                                     20011204 <--
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                                 20020613
                                             CA 2001-2431160
                                                                     20011205 <--
     AU 2002020195
                          Α5
                                 20020618
                                             AU 2002-20195
                                                                     20011205 <--
     EP 1349841
                          A2
                                 20031008
                                             EP 2001-999564
                                                                     20011205 <--
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004523497
                          T2
                                 20040805
                                             JP 2002-547910
                                                                     20011205
PRIORITY APPLN. INFO.:
                                             US 2000-251816P
                                                                  P
                                                                     20001206
                                             WO 2001-US46403
                                                                  W
                                                                    20011205
OTHER SOURCE(S):
                         MARPAT 137:33310
GΙ
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The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of IKK, particularly IKK-2, were prepared E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of ≤ 1 μM in the IKK-2 enzyme assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to IKK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds.

IT 434949-91-4P 434949-95-8P 434949-96-9P 434949-97-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of anilinopyrimidines as IKK inhibitors)

Ι

RN 434949-91-4 HCAPLUS

CN Piperazine, 1-acetyl-4-[4-[4-[4-[4-(1-pyrrolidinyl)-1 piperidinyl]sulfonyl]phenyl]-2-pyrimidinyl]amino|benzoyl]- (9CI) (CA
 INDEX NAME)

RN 434949-95-8 HCAPLUS

CN Piperazine, 1-acetyl-4-[4-[4-[4-[(2-methyl-1-piperidinyl)sulfonyl]phenyl]-2-pyrimidinyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

RN 434949-96-9 HCAPLUS

CN Piperazine, 1-acetyl-4-[4-[4-[4-[4-[4-methyl-1-piperidinyl)sulfonyl]phenyl]-2-pyrimidinyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

RN 434949-97-0 HCAPLUS

CN Piperazine, 1-acetyl-4-[4-[4-[4-[(3-methyl-1-piperidinyl)sulfonyl]phenyl]-2-pyrimidinyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

L32 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:314395 HCAPLUS

DOCUMENT NUMBER:

136:335540

TITLE:

Use of PDE V inhibitors for improved fecundity in

mammals

INVENTOR(S):

Westbrook, Simon Lempriere; Zanzinger, Johannes

Friedrich

PATENT ASSIGNEE(S):

Pfizer Limited, UK; Pfizer Inc.

SOURCE:

Eur. Pat. Appl., 20 pp.

DOCUMENT TYPE:

CODEN: EPXXDW Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PA	rent :	NO.			KIN)	DATE			APPL	ICAT	ION 1	NO.	DATE				
EP	1199	070			A2			0424]	EP 2	001-	3086	84			2001	1011	<
EP	1199	070			A 3		2004											
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		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR							
CA	2359	383			AA		2002	0420	(CA 2	2001-	2359	383			2001	1018	<
US	2003	0180	36		A1		2003	0123	1	JS 2	2001-	9824	45			2001	1018	<
US	6548	508			B2		2003	0415										
JР	2002	2203	46		A2		2002	0809	,	JP 2	2001-	3221	95			2001	1019	<
ZA	2001	0086	17		Α		2003	0422	:	ZA 2	2001-	8617				2001	1019	<
NZ	5149	47			Α		2005	0324	1	NZ 2	2001-	5149	47			2001	1019	
	2003		37		A1		2003	0123	1	US 2	2002-	2295	34			2002	0827	< - -
US	6743	799	_		В2		2004	0601										
	2004		95		A1		2004	0826	1	US 2	2004 -	7788	66			2004	0212	
PRIORIT				. :						GB 2	2000-	2578	2		A	2000	1020	
INIONII									1	US 2	2000-	2533	38P		P	2000	1128	
											2001-				A1	2001	1018	
											2002-					2002		
												-						

The invention relates to the use of a cyclic guanosine 3',5'-monophosphate phosphodiesterase type five (cGMP PDE V) inhibitor for increasing fecundity in a mammal by one or more of (a) promoting the growth of an oocyte, zygote, blastocyst, embryo and/or fetus, (b) increasing the rate or probability of survival of an embryo and/or fetus and (c) increasing the birth weight of a progeny, or for increasing milk productivity. I.v. and tablet formulations are exemplified. Formulations and packs containing the PDE V inhibitors for pharmaceutical or veterinary use are claimed.

IT 155879-56-4 224785-86-8 224786-98-5 224787-20-6 224787-26-2 224787-70-6

224787-95-5 224788-35-6 224788-38-9

224788-62-9 264912-89-2 264913-07-7

264913-09-9

RL: AGR (Agricultural use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (use of PDE V inhibitors for improved fecundity in mammals)

Ward 10_663042

RN 155879-56-4 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[3-(1,4-dihydro-4-oxo-8-propylpyrido[3,2-d]pyrimidin-2-yl)-4-ethoxyphenyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 224785-86-8 HCAPLUS

CN 3-Pyrrolidinol, 1-[[3-(1,4-dihydro-5,7-dimethyl-4-oxoimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-3-(methoxymethyl)- (9CI) (CA INDEX NAME)

RN 224786-98-5 HCAPLUS

CN 1,4'-Bipiperidine, 1'-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 224787-20-6 HCAPLUS

CN 4-Piperidinemethanol, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-phenyl-(9CI) (CA INDEX NAME)

RN

224787-26-2 HCAPLUS
Pyrrolidine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-CN f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-3-(2-pyridinyl)- (9CI) (CA INDEX NAME)

224787-70-6 HCAPLUS RN

Piperidine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-CN f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

RN 224787-95-5 HCAPLUS

1,4'-Bipiperidine, 1'-[[4-ethoxy-3-(5-ethyl-1,4-dihydro-4-oxo-7-CN propylimidazo[5,1-f][1,2,4]triazin-2-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 224788-35-6 HCAPLUS

CN Piperidine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 224788-38-9 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-, ethylester (9CI) (CA INDEX NAME)

RN 224788-62-9 HCAPLUS

CN 4-Piperidinemethanol, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]- α -(4-fluorophenyl)- (9CI) (CA INDEX NAME)

RN

264912-89-2 HCAPLUS Piperidine, 1-[[4-ethoxy-3-[3-ethyl-4,7-dihydro-7-oxo-2-(2-CN pyridinylmethyl) -2H-pyrazolo[4,3-d]pyrimidin-5-yl]phenyl]sulfonyl]-4-ethyl-(CA INDEX NAME)

264913-07-7 HCAPLUS RN

Piperidine, 4-ethyl-1-[[5-[3-ethyl-4,7-dihydro-7-oxo-2-(2-pyridinylmethyl)-CN 2H-pyrazolo[4,3-d]pyrimidin-5-yl]-6-(2-methoxyethoxy)-3pyridinyl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Et} \\ \\ \text{N} \\ \\ \text{O} \\ \text{S} \\ \text{O} \\ \\ \text{N} \\ \\$$

264913-09-9 HCAPLUS RN

3-Azetidinamine, 1-[[5-[4,7-dihydro-7-oxo-3-propyl-2-(2-pyridinylmethyl)-CN 2H-pyrazolo[4,3-d]pyrimidin-5-yl]-6-ethoxy-3-pyridinyl]sulfonyl]-N-ethyl-(9CI) (CA INDEX NAME)

HCAPLUS COPYRIGHT 2005 ACS on STN L32 ANSWER 11 OF 35

ACCESSION NUMBER:

2002:213823 HCAPLUS

DOCUMENT NUMBER:

136:247500

TITLE:

Preparation of alkynyloxyphenylsulfonylmethylpiperidin

ehydroxamic acids and related compounds as inhibitors of matrix metalloproteinase and

TNF- α converting enzyme (TACE).

INVENTOR(S):

Levin, Jeremy I.; Venkatesan, Aranapakam M.; Chen, James M.; Zask, Arie; Sandanayaka, Vincent P.; Du,

Mila T.; Baker, Jannie L.

PATENT ASSIGNEE(S):

American Cyanamid Company, USA

SOURCE:

U.S., 50 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6358980	B1	20020319	US 2000-492686	20000127. <
US 2002086890	A1	20020704	US 2001-29655	20011221 <
US 6753337	B2	20040622		
US 2004229924	A 1	20041118	US 2004-870839	20040617
PRIORITY APPLN. INFO.:			US 1999-155184P P	19990127
			US 2000-492686 A	3 20000127
			US 2001-29655 A	1 20011221

OTHER SOURCE(S): MARPAT 136:247500

R1C.tplbond.CCR2R3XYACR8R9(CR10R11)nCONR12OH (R1 = H, aryl, heteroaryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl; R2, R3 = H, alkyl, cyano, CCH; R8-R11 = H, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, alkyl, alkenyl, alkynyl; 1 of R8R9, R9R10, or R10R11 = atoms to form a cycloalkyl ring or a cycloheteroalkyl ring; R12 = H, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, alkyl; A, X = O, S, SO, SO2, NR7, CH2; R7 = H, aryl, aralkyl, heteroaryl, heteroaralkyl, etc.; Y = aryl, heteroaryl; A and X are not bonded to adjacent atoms of Y; n = 0-2), were prepared Thus, 1-acetyl-4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-4piperidinecarboxamide (preparation in several steps from Et isonipecotate given) inhibited TACE with IC50 = 4.8 nM.

IT 287201-30-3P, 4-Piperidinecarboxamide, 4-[[[4-(2butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-1-[(1-methyl-1H-pyrazol-4-

yl)sulfonyl]-RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and related compds. as **inhibitors** of matrix metalloproteinase and $TNF-\alpha$ converting **enzyme** (TACE))

RN 287201-30-3 HCAPLUS

CN 4-Piperidinecarboxamide, 4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-1-[(1-methyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

$$O-CH_2-C = C-Me$$

IT 287202-66-8P, 4-Piperidinecarboxylic acid, 4-[[4-(2-butynyloxy)phenyl]sulfonyl]-1-[(4-methoxyphenyl)sulfonyl]-, methylester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and related compds. as **inhibitors** of matrix metalloproteinase and $TNF-\alpha$ converting **enzyme** (TACE))

RN 287202-66-8 HCAPLUS

CN 4-Piperidinecarboxylic acid, 4-[[4-(2-butynyloxy)phenyl]sulfonyl]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

73

REFERENCE COUNT: THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:171694 HCAPLUS

DOCUMENT NUMBER:

136:232208

TITLE:

Preparation of 4-aminoazepan-3-one parasitic cysteine

protease inhibitors effective against malaria and

other diseases

INVENTOR(S):

Tew, David G.; Thompson, Scott K.; Veber, Daniel F.

Smithkline Beecham Corporation, UK

SOURCE:

PCT Int. Appl., 220 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT ASSIGNEE(S):

PA'	PATENT NO.						KIND DATE			APPLICATION NO.											
WO	2002	 0179	 24				2002	0307								0010	831	<			
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,				
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		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	ΝZ,	PH,	PL,				
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,				
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		ВJ,	CF,	CG,	CI,	-	GA,	-				-	•		•						
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EP	1320																				
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							RO,														
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OTHER SO	OURCE	(S):			MARI	PAT	136:	23220	80												

GI

$$R^1$$
 R''
 R^2
 R^4
 R^4
 R^2
 R^4
 R^4

The present invention relates to methods of treating parasitic diseases AB which are mediated by cysteine proteases by administration of 4-aminoazepan-3-one protease inhibitors I (e.g. benzo[1,3]dioxole-5carboxylic acid [(S)-1-(1-benzyl-3-oxoazepan-4-ylcarbamoyl)-3methylbutyl]amide) and pharmaceutically acceptable salts, hydrates and solvates thereof. In particular, the present invention relates to a method of treating malaria by inhibiting the cysteine protease falcipain. Other diseases against which the claimed compds. are effective include trypanosomiasis (African sleeping sickness, Chagas disease), leishmaniasis, schistosomiasis, onchocerciasis (river blindness) and qiardiasis. In I: R1 is R4NR'CHR3C(O)-, R5XCHR3C(O)-, R3CH2C(O)-R4NR'CR''''R3C(O)-, II. R2 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R9C(0)-, R9C(S)-, R9SO2-, R9OC(O)-, ${\tt R9R11NC(O)-,\ R9R11NC(S)-,\ R9\,(R11)\,NSO2-,\ 3-(2-pyridyl)\,benzylcarbonyl,}$ 2-(3-(2-pyridy1)pheny1)ethy1, R7NR6CHR8Z-, and R9SO2R11NC(O)-. R3 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, C2-6alkenyl, C2-6alkynyl, HetCO-6alkyl and ArCO-6alkyl. R3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring. R4 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R5C(O)-, R5C(S)-, R5SO2-, R5OC(O)-, R5R12NC(O)-, and R5R12NC(S)-. R5 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl and Het-CO-6alkyl. R6 is H, C1-6alkyl, Ar-CO-6alkyl, and Het-CO-6alkyl. is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R10C(O) -, R10C(S) -, R10SO2 -, R10OC(O) -, R10R13NC(O) -, and R10R13NC(S) -. R8 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and Arco-6alkyl. R9, R10 independently = C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl and Het-C0-6alkyl. R11, R12, R13, R', R' independently = H, C1-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl. R'' is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl; R'''' is C1-6alkyl, C3-6cycloalkyl-C0-6alkyl C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and ArCO-6alkyl. X is CH2, S, and O; Z is C(O) and CH2; n is 1-5. Although the methods of preparation are not claimed, 220 example prepns. are included.

1T 403700-46-9P, [(1S)-1-[(1-Benzenesulfonyl-3-hydroxy-7-methylazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 403700-47-0P, (S)-2-Amino-4-methylpentanoic acid [1-(2-pyridine)sulfonyl-3-hydroxy-7-methylazepan-4-yl]amide 403700-48-1P, Benzofuran-2-carboxylic acid [(1S)-1-[[3-hydroxy-7-methyl-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]-3-methylbutyl]amide RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of 4-aminoazepan-3-one parasitic cysteine protease inhibitors effective against malaria and other diseases)

RN 403700-46-9 HCAPLUS

CN

Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-7-methyl-1-(phenylsulfonyl)-

1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 403700-47-0 HCAPLUS

CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 403700-48-1 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 281215-23-4P, 5,6-Dimethoxybenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[3-oxo-1-(1-methyl-1H-imidazole-4-sulfonyl)azepan-4-yl]carbamoyl]butyl]amide 281215-25-6P, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[1-(1-methyl-1H-imidazole-2-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide 281215-28-9P, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide 281215-33-6P, 5-Hydroxybenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide 281216-87-3P,

Ward 10 663042

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Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[1-(6-methylpyridin-2-
ylsulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide 281216-98-6P,
Thieno[3,2-b]thiophene-2-carboxylic acid [(1S)-3-methyl-1-[[1-(3-
methylpyridine-2-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide
281216-99-7P, 3-Methylbenzofuran-2-carboxylic acid
[(1S)-3-methyl-1-[[1-(3-methylpyridin-2-ylsulfonyl)-3-oxoazepan-4-
yl]carbamoyl]butyl]amide 281217-04-7P, Benzofuran-2-carboxylic
acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridinesulfonyl)azepan-4-
yl]carbamoyl]butyl]amide 362505-86-0P, Benzofuran-2-carboxylic
acid [(1S)-3-methyl-1-[[(4S,7S)-7-methyl-3-oxo-1-(pyridin-2-
ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide 362505-88-2P,
Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[(4R,7R)-7-methyl-3-oxo-1-
(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide
403606-21-3P, 5-Methoxybenzofuran-2-carboxylic acid
[(1S)-3-methyl-1-[[(4R)-1-(3-methylpyridin-2-ylsulfonyl)-3-oxoazepan-4-
yl]carbamoyl]butyl]amide 403606-31-5P, Benzofuran-2-carboxylic
acid [(1S)-3-methyl-1-[[1-(2-methylfuran-3-sulfonyl)-3-oxoazepan-4-
yl]carbamoyl]butyl]amide 403606-46-2P, Benzo[b]thiophene-2-
carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridin-2-
ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide 403606-47-3P,
5-Methoxybenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-
(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide
403606-48-4P, 3-Methylbenzofuran-2-carboxylic acid
[(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-
yl]carbamoyl]butyl]amide 403606-49-5P, Thieno[3,2-b]thiophene-2-
carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridin-2-
ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide 403606-64-4P,
5-Methoxybenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[(4S)-1-(3-
methylpyridin-2-ylsulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
   (preparation of 4-aminoazepan-3-one parasitic cysteine protease
   inhibitors effective against malaria and other diseases)
281215-23-4 HCAPLUS
2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-4-
yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5,6-
```

Absolute stereochemistry.

dimethoxy- (9CI)

RN

CN

(CA INDEX NAME)

RN 281215-25-6 HCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-2-yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI)
(CA INDEX NAME)

RN 281215-28-9 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 281215-33-6 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-hydroxy-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 281216-87-3 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(6-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-(9CI) (CA INDEX NAME)

RN 281216-98-6 HCAPLUS

CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 281216-99-7 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 281217-04-7 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

RN 362505-86-0 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7S)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 362505-88-2 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 403606-21-3 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

RN 403606-31-5 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(2-methyl-3-furanyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 403606-46-2 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 403606-47-3 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy-(9CI) (CA INDEX NAME)

RN 403606-48-4 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 403606-49-5 HCAPLUS

CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 403606-64-4 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS 2 REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:90005 HCAPLUS

DOCUMENT NUMBER:

136:151068

TITLE:

Preparation of pyrrolidinethiols and analogs as

metalloprotease inhibitors

INVENTOR(S):

Aebi, Johannes; Bur, Daniel; Chucholowski, Alexander;

Dehmlow, Henrietta; Kitas, Eric Argirios; Obst,

Ulrike; Wessel, Hans Peter

PATENT ASSIGNEE(S):

F. Hoffmann-La Roche A.-G., Switz.

SOURCE:

PCT Int. Appl., 160 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

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FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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		GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	NZ,	PL,	PT,	
		RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	UΖ,	
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		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG			
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OTHER S	OURCE	(S):			MAR	PAT	136:	1510	68									

OTHER SOURCE(S):

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AB Title compds. [e.g., I; R = Z1R3 or SO3H; R1 = H, alkanoyl, aroyl; R3 = alkyl, (hetero)aryl, heterocyclyl, etc.; R4 = H or alkyl; R5 = CH2Z2R2; R2 = aryl(alkyl), ar(o)ylamino, arylsulfonyl, etc.; Z1 = sulfonyl(amino), CONH, CO2, etc.; Z2 = CH2, O, S, (un)substituted NH] were prepared Thus, e.g., (3R,5S)-1-naphthalene-2-sulfonyl-5-anilinomethylpyrrolidine-3-thiol was prepared Data for biol. activity of title compds. were given.

IT 393787-19-4P 393787-20-7P 393787-89-8P 393787-90-1P 393787-91-2P 393787-92-3P 393788-00-6P 393788-02-8P 393788-04-0P 393788-18-6P 393788-20-0P 393788-27-7P 393790-15-3P 393790-17-5P 393790-19-7P 393790-20-0P 393790-21-1P 393790-22-2P 393790-23-3P 393790-24-4P 393790-26-6P 393790-27-7P 393790-28-8P 393790-29-9P 393790-32-4P 393790-34-6P 393790-35-7P 393790-36-8P 393790-39-1P 393790-45-9P 393790-46-0P 393790-47-1P 393791-26-9P 393791-27-0P 393791-28-1P 393791-29-2P 393791-32-7P 393791-33-8P 393791-34-9P 393791-36-1P 393791-37-2P 393791-42-9P 393791-43-0P 393791-44-1P 393793-31-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolidinethiols and analogs as metalloprotease inhibitors)

RN 393787-19-4 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4R)-4-mercapto-1-(2naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-, ethyl ester (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

RN 393787-20-7 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-(1-piperidinylmethyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393787-89-8 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(4-acetyl-5-methyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393787-90-1 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 1-[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-5-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 393787-91-2 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(5-methyl-4-phenyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393787-92-3 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(5-amino-4-phenyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393788-00-6 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 1-[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-5-methyl- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.

RN 393788-02-8 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 5-amino-1-[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393788-04-0 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[2-(5-methyl-4-phenyl-1H-1,2,3-triazol-1-yl)ethyl]-1-(2-naphthalenylsulfonyl)-, (3R,5R)- (9CI) (CA INDEX NAME)

RN 393788-18-6 HCAPLUS

CN 2-Pyrrolidineethanol, 4-mercapto-1-(2-naphthalenylsulfonyl)-, α -(phenylcarbamate), (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393788-20-0 HCAPLUS

CN Glycine, N-[[2-[(2R,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2 pyrrolidinyl]ethoxy]carbonyl]-N-phenyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393788-27-7 HCAPLUS

CN 3-Pyrrolidinethiol, 5-(methoxymethyl)-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-15-3 HCAPLUS

CN 2H-3,1-Benzoxazine-2,4(1H)-dione, 1-[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME) Absolute stereochemistry.

RN 393790-17-5 HCAPLUS

CN Benzoic acid, 2-amino-5-[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-19-7 HCAPLUS

CN Benzoic acid, 2-amino-5-[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 393790-20-0 HCAPLUS

CN Acetamide, N-[4-[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-21-1 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(3-nitrophenyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-22-2 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(2-nitrophenyl)sulfonyl]-5-[(phenylmethoxy)methyl], (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-23-3 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[[4-(methylsulfonyl)phenyl]sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-24-4 HCAPLUS

CN 3-Pyrrolidinethiol, 1-([1,1'-biphenyl]-4-ylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-26-6 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-5-

[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-27-7 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(phenylmethoxy)methyl]-1-(2-thienylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-28-8 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(phenylmethoxy)methyl]-1-(phenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-29-9 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(3-chlorophenyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

RN 393790-32-4 HCAPLUS CN 3-Pyrrolidinethiol, 1-[(4-fluorophenyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-34-6 HCAPLUS CN 3-Pyrrolidinethiol, 5-[(phenylmethoxy)methyl]-1-(8-quinolinylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-35-7 HCAPLUS
CN 3-Pyrrolidinethiol, 1-[(1,4-dihydro-2,4-dioxo-2H-3,1-benzoxazin-6yl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

RN 393790-36-8 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-thienylsulfonyl)-5-[[(2,3,5-trifluorophenyl)methoxy]methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-39-1 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(1-naphthalenylsulfonyl)-5-[[(2,3,5-trifluorophenyl)methoxy]methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

RN 393790-45-9 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(8-quinolinylsulfonyl)-5-[[(2,3,5-trifluorophenyl)methoxy]methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-46-0 HCAPLUS

CN Acetamide, N-[4-[[(2S,4R)-4-mercapto-2-[[(2,3,5-trifluorophenyl)methoxy]methyl]-1-pyrrolidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393790-47-1 HCAPLUS

CN Benzoic acid, 2-ethoxy-5-[[(2S,4R)-4-mercapto-2-[[(2,3,5-trifluorophenyl)methoxy]methyl]-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 393791-26-9 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[3-(4-fluorophenyl)propyl]-1-(2-naphthalenylsulfonyl)-, (3R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393791-27-0 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393791-28-1 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 393791-29-2 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, (3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393791-32-7 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393791-33-8 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-

pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393791-34-9 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393791-36-1 HCAPLUS

CN Piperidine, 3-(methylthio)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393791-37-2 HCAPLUS

CN Piperidine, 2-(methylthio)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (2R,5R)-rel- (9CI) (CA INDEX NAME)

RN 393791-42-9 HCAPLUS

CN Pyrrolidine, 3-(methylthio)-1-(2-naphthalenylsulfonyl)-4[(phenylmethoxy)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393791-43-0 HCAPLUS

CN 4-Piperidinethiol, 1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-, (3R,4S)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393791-44-1 HCAPLUS

CN 4-Piperidinethiol, 1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-31-2 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-,

(3S, 5R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 393793-82-3

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of pyrrolidinethiols and analogs as metalloprotease
 inhibitors)

RN 393793-82-3 HCAPLUS

CN D-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

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IT
     391671-83-3P 391671-85-5P 391671-90-2P
     391671-92-4P 391672-17-6P 391672-19-8P
     393153-99-6P 393792-17-1P 393792-19-3P
     393792-20-6P 393792-21-7P 393792-22-8P
     393792-26-2P 393792-27-3P 393792-28-4P
     393792-63-7P 393793-01-6P 393793-02-7P
     393793-06-1P 393793-07-2P 393793-08-3P
     393793-09-4P 393793-13-0P 393793-14-1P
     393793-15-2P 393793-18-5P 393793-19-6P
     393793-20-9P 393793-23-2P 393793-24-3P
     393793-25-4P 393793-27-6P 393793-28-7P
     393793-29-8P 393793-33-4P 393793-34-5P
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     393793-40-3P 393793-41-4P 393793-42-5P
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     393793-48-1P 393793-51-6P 393793-60-7P
     393793-61-8P 393793-63-0P 393793-64-1P
     393793-65-2P 393793-69-6P 393793-70-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of pyrrolidinethiols and analogs as metalloprotease
        inhibitors)
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RN 391671-83-3 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391671-85-5 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391671-90-2 HCAPLUS

CN L-Proline, 4-[(methylsulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391671-92-4 HCAPLUS

CN L-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 391672-17-6 HCAPLUS

CN L-Proline, 4-bromo-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391672-19-8 HCAPLUS

CN L-Proline, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393153-99-6 HCAPLUS

CN 2-Pyrrolidineacetic acid, 1-(2-naphthalenylsulfonyl)-4[(triphenylmethyl)thio]-, methyl ester, (2R,4R)- (9CI) (CA INDEX NAME)

RN 393792-17-1 HCAPLUS

CN L-Proline, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393792-19-3 HCAPLUS

CN Pyrrolidine, 2-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(2-naphthalenylsulfonyl)-, (2S,4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393792-20-6 HCAPLUS

CN 3-Pyrrolidinol, 5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

RN 393792-21-7 HCAPLUS

CN 3-Pyrrolidinol, 5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-1-(2-naphthalenylsulfonyl)-, methanesulfonate (ester), (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393792-22-8 HCAPLUS

CN Ethanethioic acid, S-[(3R,5S)-5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-1-(2-naphthalenylsulfonyl)-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393792-26-2 HCAPLUS

CN Pyrrolidine, 2-[(4-acetyl-5-methyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, (2S,4R)- (9CI) (CA

INDEX NAME)

Absolute stereochemistry.

RN 393792-27-3 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 1-[[(2S,4R)-4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-5-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393792-28-4 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxamide, 5-amino-1-[[(2S,4R)-4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]- (9CI) (CA INDEX NAME)

RN393792-63-7 HCAPLUS

CN2H-3,1-Benzoxazine-2,4(1H)-dione, 1-[[(2S,4R)-2-[(phenylmethoxy)methyl]-4-[(triphenylmethyl)thio]-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

393793-01-6 HCAPLUS
Pyrrolidine, 2-[3-(4-fluorophenyl)-3-oxopropyl]-4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, (2R,4R)- (9CI) CN(CA INDEX NAME)

RN 393793-02-7 HCAPLUS

CN L-Proline, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-06-1 HCAPLUS

CN Pyrrolidine, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-[(phenylmethoxy)methyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-07-2 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4R)-4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 393793-08-3 HCAPLUS

CN Pyrrolidine, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-[[[(2E)-3-phenyl-2-propenyl]oxy]methyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 393793-09-4 HCAPLUS

CN Pyrrolidine, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-[(3-phenylpropoxy)methyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-13-0 HCAPLUS

CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

RN 393793-14-1 HCAPLUS

CN Benzoic acid, 3-[[(2R,4S)-4-hydroxy-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-15-2 HCAPLUS

CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-18-5 HCAPLUS

CN Ethanethioic acid, S-[(3S,5S)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

RN 393793-19-6 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4S)-4-(acetylthio)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-20-9 HCAPLUS

CN Ethanethioic acid, S-[(3S,5S)-1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-23-2 HCAPLUS

CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, methanesulfonate (ester), (3S,5S)- (9CI) (CA INDEX NAME)

RN 393793-24-3 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4S)-4-[(methylsulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-25-4 HCAPLUS

CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, methanesulfonate (ester), (3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-27-6 HCAPLUS

CN Ethanethioic acid, S-[(3S,5R)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

RN 393793-28-7 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4R)-4-(acetylthio)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-29-8 HCAPLUS

CN Ethanethioic acid, S-[(3R,5S)-1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393793-33-4 HCAPLUS

CN 2,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, dimethyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

RN 393793-34-5 HCAPLUS

CN 3,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, dimethyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-36-7 HCAPLUS

CN 2,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, 2-methyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-37-8 HCAPLUS

CN 3,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, monomethyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

RN 393793-39-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 5-(hydroxymethyl)-1-(2-naphthalenylsulfonyl)-, methyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-40-3 HCAPLUS

CN 3-Piperidinecarboxylic acid, 5-(hydroxymethyl)-1-(2-naphthalenylsulfonyl)-, methyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-41-4 HCAPLUS

CN 3-Piperidinecarboxylic acid, 1-(2-naphthalenylsulfonyl)-5[(phenylmethoxy)methyl]-, methyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

RN 393793-42-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, methyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-44-7 HCAPLUS
CN 3-Piperidinemethanol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl], (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-45-8 HCAPLUS
CN 2-Piperidinemethanol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl], (2R,5R)-rel- (9CI) (CA INDEX NAME)

RN 393793-47-0 HCAPLUS

CN Ethanethioic acid, S-[[(3R,5S)-1-(2-naphthalenylsulfonyl)-5[(phenylmethoxy)methyl]-3-piperidinyl]methyl] ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-48-1 HCAPLUS

CN Ethanethioic acid, S-[[(2R,5R)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-2-piperidinyl]methyl] ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-51-6 HCAPLUS

CN 3,4-Pyrrolidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, diethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

RN

393793-60-7 HCAPLUS
Pyrrolidine, 1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-4-CN [[(triphenylmethyl)thio]methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN393793-61-8 HCAPLUS

3-Pyridinecarboxylic acid, 1,2,5,6-tetrahydro-4-hydroxy-1-(2-CN naphthalenylsulfonyl) -, ethyl ester (9CI) (CA INDEX NAME)

RN393793-63-0 HCAPLUS

3-Piperidinecarboxylic acid, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, ethyl CN ester, (3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

393793-64-1 HCAPLUS RN

CN 3-Piperidinecarboxylic acid, 4-[(methylsulfonyl)oxy]-1-(2naphthalenylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 393793-65-2 HCAPLUS

CN 3-Piperidinecarboxylic acid, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & & & & \\ \hline & S & & & \\ S & & & \\ \hline & & & \\ O & & & \\ \hline & & & \\ O & & \\ \end{array}$$

RN 393793-69-6 HCAPLUS

CN Piperidine, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-, (3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 393793-70-9 HCAPLUS

CN Piperidine, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS 10 REFERENCE COUNT:

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

2002:72039 HCAPLUS ACCESSION NUMBER:

136:118380 DOCUMENT NUMBER:

Pyrrolidine-2-carboxylic acid hydrazide derivatives TITLE:

for use as metalloprotease inhibitors

Aebi, Johannes; Dehmlow, Henrietta; Kitas, Eric INVENTOR(S):

Argirios

F. Hoffmann-La Roche A.-G., Switz. PATENT ASSIGNEE(S):

PCT Int. Appl., 78 pp. SOURCE:

CODEN: PIXXD2

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US 2002040048	A1 20020404	US 2001-900350	20010706 <				
	B2 20020903						
CA 2415665	AA 20020124	CA 2001-2415665	20010711 <				
EP 1317428	A1 20030611	EP 2001-954031	20010711 <				
R: AT, BE,	H, DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,				
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		BR 2001-12543	20010711 <				
TP 2004504298	T2 20040212	JP 2002-512130	20010711				
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GΙ

AB Title compds. I [R1 = H, acyl; R2 = (un)substituted alkyl, cycloalkyl, akynyl, aryl, heterocyclic; R3 = H, aryl, alkyl, aralkyl, arylsulfonyl, heteroarylsulfonyl; R4 = H, aralkyl, alkyl, aryl, cycloalkyl, cycloalkylalkyl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, heteroarylsulfonyl, carboxyalkyl, carboxyalkylsulfonyl, alkoxycarbonyalkyl; NR4R5, R3NNR4R5 = heterocyclic; R5 = H, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkoxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, acyl, heterocyclyl, (un)substituted aminosulfonyl, aminoalkylcarbonyl, arylcarbamoyl, alkyl, acyl, alkoxycarbonyl, aryl, aralkyl, arylalkoxycarbonyl, heteroaryl; X = SO2, SO2NH, CO, (un) substituted CONH, CO2] were prepared for use as inhibitors of metalloproteases, e.g. zinc proteases, particularly zinc hydrolases, and are effective in treating disease states are associated with vasoconstriction of increasing occurrences. Thus, (2S,4R)-I [X = SO2, R1, R3 = H, R2 = 2-naphthyl, NR4R5 = 2-oxopyrrolidino] was prepared from L-hydroxyproline Me ester hydrochloride in 7 steps.

IT 391671-83-3P 391671-85-5P 391671-90-2P 391671-92-4P 391672-17-6P 391672-19-8P 391672-22-3P 391673-01-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrrolidine-2-carboxylic acid hydrazide derivs. for use as metalloprotease inhibitors)

RN 391671-83-3 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391671-85-5 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 391671-90-2 HCAPLUS

CN L-Proline, 4-[(methylsulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391671-92-4 HCAPLUS

CN L-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391672-17-6 HCAPLUS

CN L-Proline, 4-bromo-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4S)-(9CI) (CA INDEX NAME)

RN 391672-19-8 HCAPLUS

CN L-Proline, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391672-22-3 HCAPLUS

CN L-Proline, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391673-01-1 HCAPLUS

CN 3(2H)-Pyridazinone, tetrahydro-1-[[(2S,4R)-1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

IT 391673-03-3P 391673-66-8P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolidine-2-carboxylic acid hydrazide derivs. for use as metalloprotease inhibitors)

RN 391673-03-3 HCAPLUS

CN 3(2H)-Pyridazinone, tetrahydro-1-[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391673-66-8 HCAPLUS

CN L-Proline, 1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-4-mercapto-, 2-[(4-methylphenyl)sulfonyl]hydrazide, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

2

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Ward 10 663042

L32 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:72037 HCAPLUS

DOCUMENT NUMBER: 136:134667

TITLE: Preparation of mercaptopyrrolidinecarboxamides related

compounds as inhibitors of endothelin-converting enzyme

INVENTOR(S): Aebi, Johannes; Blum, Denise; Bur, Daniel;

Chucholowski, Alexander; Dehmlow, Henrietta; Kitas, Eric Argirios; Loeffler, Bernd Michael; Obst, Ulrike;

Wallbaum, Sabine

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE:

PCT Int. Appl., 160 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.						APPLICATION NO.											
	WO 2002006222													2	0010	710	<	
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KΡ,	KR,	KZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	
							SI,											
		-			-		AZ,				•					•		
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY	
		•	•		-		GB,				•		•		•			
		•	•			-	GA,		•	•	•	•		•	•	•		
CA	2414	311	•	•	AΑ	•	2002	0124	•	CA 2	001-	2414	311	•	2	0010	710	<
EP	1303	485			A1		2003	0423		EP 2	001-	9494	85		2	0010	710	<
							ES,											
			•		-		RO,				•	•	•	•		•		
BR	2001	•	•	•	•		•	•	•	•		1258	0		2	0010	710	<
JP	2004	5042	97		Т2		2004	0212		JP 2	002-	5121	28		2	0010	710	
US	2002	0492	43		A1		2002	0425		US 2	001-	9071	35		2	0010		<
	6541						2003								_		. – .	
	2003									ZA 2	003-	167			2	0030	107	
PRIORIT																		
														1		0010		
OTHER SO		(S):			MAR	TAG	136:	1346		2		, ,		'			0	

Ι

AB Title compds. [I; R1 = H, alkylcarbonyl, arylcarbonyl; R2 = alkyl, alkylcycloalkyl, cycloalkyl, haloalkyl, carboxyalkyl, aryl, alkynyl, aryloxyalkyl, heterocyclyl, etc.; A = COR3, CH(OH)R4, CONR5R6; R3, R4 = alkyl, aryl, arylalkynyl, aralkyl, arylalkenyl; R5 = H, alkyl, cycloalkyl,

Ward 10 663042

cycloalkylalkyl, carboxyalkyl, aralkyl; R6 = alkyl, alkylcarbonylalkyl, cyanoalkyl, hydroxyalkyl, aminocarbonylalkyl, aryl, etc.; m = 0-2; X = SO2, CO, CO2, SO2NH, CONR13; R13 = H, alkyl, aryl, carboxyalkyl], and dimers thereof, were prepared Thus, (2S,4R)-[[4-(4-methoxybenzylsulfanyl)-1-(naphthalene-2-sulfonyl)pyrrolidine-2-carbonyl]methylamino]acetic acid (preparation given) in CH2Cl2 were treated with NMM, HOBT in CH2Cl2, EDCI in CH2Cl2, and o-toluidine in CH2Cl2; the solution was shaken overnight to give a residue which was treated with Et3SiH in CF3CO2H at 80° for 1 h to give (2S,4R)-4-mercapto-1-(naphthalene-2-sulfonyl)pyrrolidine-2-carboxylic acid methyl(o-tolylcarbamoylmethyl)amide. I inhibited endothelin converting enzyme with IC50 = 5-1000 nM.

IT 393153-57-6P 393153-58-7P 393153-78-1P 393156-50-8P 393156-51-9P 393156-52-0P 393156-53-1P 393157-03-4P 393157-08-9P 393157-26-1P 393157-30-7P 393157-31-8P 393157-60-3P 393157-62-5P 393157-71-6P 393157-75-0P 393157-79-4P 393157-82-9P 393158-73-1P 393158-74-2P 393158-75-3P 393158-76-4P 393159-15-4P 393159-18-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of mercaptopyrrolidinecarboxamides as **inhibitors** of endothelin-converting **enzyme**)

RN 393153-57-6 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(2naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CF
INDEX NAME)

Absolute stereochemistry.

RN 393153-58-7 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

RN 393153-78-1 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-(acetylthio)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CAINDEX NAME)

Absolute stereochemistry.

RN 393156-50-8 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 393156-51-9 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-1-[[5-(dimethylamino)-2-naphthalenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393156-52-0 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(1-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393156-53-1 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-1-[[5-(dimethylamino)-2-naphthalenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

RN 393157-03-4 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-08-9 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-4-hydroxy-,
methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-26-1 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-4-hydroxy-,

(4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-30-7 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-31-8 HCAPLUS

CN 3-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-60-3 HCAPLUS

CN L-Proline, (4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-, methyl

ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-62-5 HCAPLUS

CN D-Proline, (4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-71-6 HCAPLUS

CN D-Proline, (4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-75-0 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4R)-4-mercapto-1-(2naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

RN 393157-79-4 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-82-9 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4R)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 393158-73-1 HCAPLUS

Piperidine, 1-[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-CN pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

393158-74-2 HCAPLUS
Piperidine, 1-[[(2S,4S)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

RN393158-75-3 HCAPLUS

Piperidine, 1-[[(2S,4S)-4-mercapto-1-[(4-methoxyphenyl)sulfonyl]-2pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

RN

393158-76-4 HCAPLUS
Piperidine, 1-[[(2S,4S)-1-[(4-butoxyphenyl)sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

RN393159-15-4 HCAPLUS

3-Pyrrolidinethiol, 5-(4-fluorobenzoyl)-1-(2-naphthalenylsulfonyl)-, CN(3R,5S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

393159-18-7 HCAPLUS RN

3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-(1-oxo-3-phenylpropyl)-, CN(3R,5S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

393156-81-5 393156-83-7 393157-14-7 IT393157-15-8 393157-17-0 393157-18-1 393157-23-8

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of mercaptopyrrolidinecarboxamides as inhibitors of endothelin-converting enzyme)

RN 393156-81-5 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[((2S,4S)-4-mercapto-1-[(4-methoxyphenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393156-83-7 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(2-thienylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-14-7 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(2naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CF
INDEX NAME)

RN 393157-15-8 HCAPLUS

CN 3-Piperidinecarboxylic acid, 1-[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-17-0 HCAPLUS

CN 4-Piperidinol, 1-[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393157-18-1 HCAPLUS

CN Acetic acid, [[1-[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-

pyrrolidinyl]carbonyl]-4-piperidinyl]oxy]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

RN 393157-23-8 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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IT 391671-83-3P 391671-85-5P 391671-90-2P
391671-92-4P 391672-17-6P 391672-19-8P
391672-22-3P 393153-80-5P 393153-82-7P
393153-83-8P 393153-84-9P 393153-92-9P
393153-93-0P 393153-99-6P 393154-04-6P
393154-69-3P 393154-78-4P 393156-49-5P
393159-07-4P 393159-08-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
```

(preparation of mercaptopyrrolidinecarboxamides as inhibitors of endothelin-converting enzyme)

RN 391671-83-3 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

RN 391671-85-5 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391671-90-2 HCAPLUS

CN L-Proline, 4-[(methylsulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391671-92-4 HCAPLUS

CN L-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 391672-17-6 HCAPLUS

CN L-Proline, 4-bromo-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391672-19-8 HCAPLUS

CN L-Proline, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 391672-22-3 HCAPLUS

CN L-Proline, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

RN 393153-80-5 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, 1,1-dimethylethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393153-82-7 HCAPLUS

CN L-Proline, 4-(acetylthio)-1-(2-naphthalenylsulfonyl)-, 1,1-dimethylethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393153-83-8 HCAPLUS

CN L-Proline, 4-(acetylthio)-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

RN 393153-84-9 HCAPLUS

CN L-Proline, 4-(acetylthio)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) · (CA INDEX NAME)

Absolute stereochemistry.

RN 393153-92-9 HCAPLUS

CN L-Proline, 4-[[(4-methylphenyl)sulfonyl]oxy]-1-(2-naphthalenylsulfonyl)-,
 methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393153-93-0 HCAPLUS

CN L-Proline, 4-(acetylthio)-1-(2-naphthalenylsulfonyl)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

RN 393153-99-6 HCAPLUS

CN 2-Pyrrolidineacetic acid, 1-(2-naphthalenylsulfonyl)-4[(triphenylmethyl)thio]-, methyl ester, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393154-04-6 HCAPLUS

CN 2-Pyrrolidinepropanoic acid, 4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, methyl ester, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393154-69-3 HCAPLUS

CN Ethanethioic acid, S-[(3S,5S)-1-(2-naphthalenylsulfonyl)-5-(1-piperidinylcarbonyl)-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

RN 393154-78-4 HCAPLUS

CN Pyrrolidine, 2-(4-methoxybenzoyl)-4-[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393156-49-5 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1,1'-[dithiobis[[(2S,4S)-1-(2-naphthalenylsulfonyl)-4,2-pyrrolidinediyl]carbonyl]]bis-, diethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 393159-07-4 HCAPLUS CN 3-Pyrrolidinethiol, 5-(4-methoxybenzoyl)-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 393159-08-5 HCAPLUS

CN 3-Pyrrolidinethiol, 5-benzoyl-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:6377 HCAPLUS

DOCUMENT NUMBER:

136:69695

TITLE:

Preparation of β -lactam compounds as inhibitors

of tryptase

INVENTOR(S):

Bisacchi, Gregory S.; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven; Kronenthal, David R.; Randazzo, Michael E.; Schwinden,

Mark D.; Xu, Zhongmin; Shi, Zhongping

PATENT ASSIGNEE(S):

Bristol-Myers Squibb Co., USA

SOURCE:

U.S., 171 pp., Cont.-in-part of U.S. Ser. No.

336,253, abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6335324 PRIORITY APPLN. INFO.:	B1	20020101		19991213 < P 19980625 B2 19990618
OTHER SOURCE(S):	MARPAT	136:69695		

$$\begin{array}{c} \text{NH} \\ \text{H}_2\text{N}-\text{C}-\text{NH} \text{ (CH}_2)_{\text{ } n} \\ \text{O} \\ \text{X} \text{ I} \end{array} \qquad \begin{array}{c} \text{NH} \cdot \text{TFA} \\ \text{H}_2\text{N} \\ \text{NH} \\ \text{NH} \\ \text{NH} \end{array} \qquad \begin{array}{c} \text{CO}_2\text{H} \\ \text{NH} \\ \text{NH} \\ \text{NH} \\ \text{NH} \end{array} \qquad \begin{array}{c} \text{CO}_2\text{H} \\ \text{NH} \\ \text{NH} \\ \text{NH} \\ \text{NH} \\ \text{NH} \end{array} \qquad \begin{array}{c} \text{CO}_2\text{H} \\ \text{NH} \\ \text{N$$

AB Novel β -lactam compds., e.g. of formula I [R = CO2H, alkoxycarbonyl, acyl, CO-heterocyclyl, etc.; X = acyl, CO-heterocyclyl, SO2-alkyl, aminoalkylphenyl, etc.; n = 1-6], are prepared These compds.

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inhibit tryptase as well as other enzyme systems or are
selective tryptase inhibitors and are useful as antiinflammatory
agents particularly in the treatment of chronic asthma (no data). Thus
II was prepared from (4S)-N-(tert-butyldimethylsilyl)azetidin-2-one-4carboxylic acid, 1-chloro-3-iodopropane, N,N'-bis(benzyloxycarbonyl)-1guanylpyrazole and benzyl isocyanate.

253174-33-3P 253174-35-5P 253174-36-6P 253174-39-9P 253174-40-2P 253174-53-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of β -lactam compds. as inhibitors of tryptase)

RN 253174-33-3 HCAPLUS

IT

CN

2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4,4-dimethyl-, monohydrochloride (9CI) (CAINDEX NAME)

● HCl

RN 253174-35-5 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 253174-34-4 CMF C15 H22 N4 O3 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 253174-36-6 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

HC1

RN 253174-39-9 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-([1,1'-biphenyl]-4-ylsulfonyl)-4,4-dimethyl-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCl

RN 253174-40-2 HCAPLUS

CN Piperidine, 1-[4-[[(3R)-3-[3-[(aminoiminomethyl)amino]propyl]-2,2-dimethyl-4-oxo-1-azetidinyl]sulfonyl]benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & \\ H_2N & & \\ NH & & \\ \end{array}$$

HCl

RN 253174-53-7 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 253174-52-6 CMF C15 H22 N4 O3 S

Absolute stereochemistry. Rotation (-).

. Me N S Ph
$$H_2N$$
 H $CH_2) $\frac{Me}{3}$ $O$$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 253176-09-9P 253176-75-9P 253176-76-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of β -lactam compds. as inhibitors of tryptase)

RN 253176-09-9 HCAPLUS

CN 2-Azetidinecarboxylic acid, 1-([1,1'-biphenyl]-4-ylsulfonyl)-3-[3-[[bis[[(phenylmethoxy)carbonyl]amino]methylene]amino]propyl]-4-oxo-, phenylmethyl ester, (2S,3R)- (9CI) (CA INDEX NAME) Absolute stereochemistry.

RN 253176-75-9 HCAPLUS

CN Carbamic acid, [[3-[(3R)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 253176-76-0 HCAPLUS

CN Carbamic acid, [[3-[(3S)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS

Ward 10_663042

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:762982 HCAPLUS

DOCUMENT NUMBER: TITLE:

135:318704 Preparation of benzimidazole-, benzoxazole- and

benzothiazolesulfonamide amino acid derivatives as

selective matrix metalloproteinase inhibitors

INVENTOR(S):

Park, Young-Jun; Bae, Hae-Young; Yoo, Ji-Uk; Chae, Myeong-Yun; Paek, Sang-Hyun; Min, Hye-Kyung; Park,

Hyun-Gyu; Ryu, Choon-Ho; Kim, Kyung-Chul; Lee,

Jeoung-Wook

PATENT ASSIGNEE(S):

Samsung Electronics Co., Ltd., S. Korea

SOURCE:

PCT Int. Appl., 115 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.				KIND DATE						ION 1		DATE							
- W	 IO	2001077092			A1 20011018			,				-	20010407 <						
	-	W:	AE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
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									KE,										
									MW,										
			SE,	SG,	SI.	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	
									ΚZ,										
		RW:							SD,					ZW,	ΑT,	BE,	CH,	CY,	,
									GR,										
									GN,										
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K	Œ	2001099526			Α		20011109 KR 2000-18328								20000407 <				
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· A	U	2001	0488	84		A 5		20011023 AU 2001-48884							20010407 <				
E	EΡ	1208							0529										
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,	,
			ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR							
J	ΙP	2003	5303	89		T2		20031014 JP 2001-575566							2	0010	407	<	
U	JS	2002	1693	14		A 1		2002	1114		US 2	001-	1850	7		2	0011	206	<
U	JS	6548	667			В2		2003	0415										
PRIORI	ORITY APPLN. INFO.:								KR 2	000-	1832	7		A 2					
											KR 2	000-	1832	8		A 2			
														1		A 2			
											WO 2	001-	KR58	5	,	W 2	0010	407	
our roo	TIED COIDCE/C).				MΛD	דעם	MADDAT 125.219704												

OTHER SOURCE(S):

MARPAT 135:318704

GI

$$x^{1-X^{2}}$$
 x^{1}
 x^{1}
 x^{1}
 x^{1}
 x^{2}
 x^{2}

$$R^{1-X^{2}}$$
 X^{1}
 SO_{2}
 $N(R)$
 $C(O)R^{5}$
 $N(R)$
 $N(R)$

AB The present invention provides novel sulfonamide derivs. (I (e.g. (2R) -3-methyl-2-[(2-phenylthiobenzothiazole-6-sulfonyl)amino]butanoic acid Me ester), II (n = 0-4) and III (n = 0-4), useful as an inhibitors of matrix metalloproteinase (MMP), its isomers, pharmaceutically acceptable salts thereof and a process for preparing the same. Since the sulfonamide derivs. of the present invention selectively inhibit MMP activity in vitro, the MMP inhibitors comprising the sulfonamide derivs. as an effective ingredient can be practically applied for the prevention and treatment of all sorts of diseases caused by overexpression and overactivation of MMP. In I: R1 denotes H, C1-12 alkyl, carbocyclic aryl-lower alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or thio) C3-7 cycloalkyl-lower alkyl, C2-12 lower alkenyl, C2-12 lower alkynyl, carbocyclic aryl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, halo lower alkyl, biaryl-lower alkylarylalkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl (thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, (N-lower alkylpiperazino, or N-carbocyclic or heterocyclic aryl-lower alkylpiperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R2 denotes H, lower alkyl, carbocyclic aryl-lower alkyl, C1-4 carbocyclic aryl-lower alkyl, C1-4 heterocyclic aryl-lower alkyl, C1-5 alkoxyphenyl-lower alkyl, C1-5 alkenoxyphenyl-lower alkyl, C1-5 alkynoxyphenyl-lower alkyl, heterocyclic aryl-lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, thio-lower alkyl, alkyl or aryl-(thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, carboxy-lower alkyl, (amino, mono or dialkylamino) lower alkyl or acylamino lower alkyl. R3 denotes H or C1-6-lower alkyl. R4 denotes H, C1-12 alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or thio) C3-7 cycloalkyl-lower alkyl, carbocyclic aryl, carbocyclic aryl-lower alkyl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, biaryl-lower alkyl, halo lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl-(thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, carboxy lower alkyl, (N-lower alkylpiperazino, or

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N-carbocyclic or heterocyclic aryl piperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R5 denotes hydroxy, alkoxy, halogen, thiol, thioalkoxy or hydroxylamine. X1 and X2 denote N-R7 (R7 is H, C1-6-lower alkyl, aryl, heteroaryl or arylalkyl), S or O. I can be prepared by (i) reacting a sulfonyl halide with H2NCR2R3CO2R6 (R6 = protecting group) in an organic solvent in the presence of a base to give a sulfonamide; (ii) replacing the H on N using R4-L (L = reactive leaving group) in an organic solvent in the presence of a base; and (iii) hydrolyzing the intermediate to give I (R5 = OH), or further condensing I (R5 = OH) to prepare I (R5 = NHOH). Alternatively, I can be prepared by (i) chlorosulfonylating IV; (ii) reacting this intermediate with an amino acid derivative in an organic solvent in the

presence

of base to give a sulfonamide; (iii) heating this intermediate and R1-X2H together at 70 to 80° in an organic solvent in the presence of base to cause substitution for Cl; (iv) reacting this intermediate with R4-L (L = reactive leaving group) in an organic solvent in the presence of base to cause substitution for H on N; and, (v) hydrolyzing this intermediate into I (R5 = OH), or further condensing I (R5= OH) to prepare I (R5 = NHOH). apprx.70 Example prepns. of intermediates and products are given. Inhibition rates for some of the claimed compds. are reported for gelatinase A (MMP-2), gelatinase B (MMP-9) and collagenase (MMP-1).

IT 367517-01-9P, (2R)-N-[2-(n-Pentylthio)benzothiazole-6-sulfonyl]-2-methoxycarbonylpyrrolidine

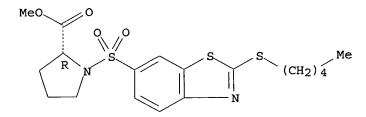
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of benzimidazole-, benzoxazole- and benzothiazolesulfonamide amino acid derivs. as selective matrix metalloproteinase inhibitors)

RN 367517-01-9 HCAPLUS

CN D-Proline, 1-[[2-(pentylthio)-6-benzothiazolyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:565008 HCAPLUS

DOCUMENT NUMBER: 135:137406

TITLE: Preparation of α -sulfonyl hydroxamic acid

derivatives as matrix metalloproteinase and TNF-alpha

converting enzyme inhibitors

INVENTOR(S): Sandanayaka, Vincent Premarana; Zask, Arie;

Venkatesan, Aranapakam Mudumbai; Baker, Jannie Lea; Krishnan, Lalitha; Megati, Sreenivasulu; Zeldis,

Joseph

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE:

PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.				KIND DATE					APPL				DATE					
	WO 2001055112														20010125 <				
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			CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	
			HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	
			LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,	
								SL,											
								KG,						-	-	-			
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								GA,									•	•	
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	ΕP	1252	143			A1		2001 2002	1030		EP 2	001-	9051	21		2	0010	125	< - -
		R:	AT,	BE,	CH,	DE,		ES,											
								RO,					•	•	•	_	•	•	
	BR	2001	0078	62		Α		2002	1105		BR 2	001-	7862			2	0010	125	<
	JP	2003	5208	52		Т2		2003	0708		JP 2	001-	5550	54		2	0010	125	<
PRIO		Y APP									US 2	000-	4929	75		A 2	0000	127	
											WO 2	001-	US26	69		W 2	0010	125	
OTHE	R S	OURCE	(S):			MAR	TAS	135:	1374								•		
AB		1YCOC									hyls	ilyl	, et	c.;	Y =	н, а	lkyl	, ar	yl,
		c.; R																	
																			alpha
		vert																	-
	inl	nibit	ors,	ren	in i :	nhib	itor	s, a	ntit	hrom	boti	cs,	and						
		lipox												step					
		nthes													idin	e-3-	carb	oxyl:	ic
		id hy							•			•		•				•	
IT		7202-				-													
	RL	RCT	(Re	acta:	nt);	SPN	(Sy	nthe	tic :	orep	arat	ion)	; PR	EP (Prep	arat	ion)	; RA	CT
		eacta					•		•				•				•	•	
							lfor	yl h	ydro:	xami	c ac	id d	eriv	s. a	s ma	trix			
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		inhi						_,	-			J -	4						
RN	287	7202-	66-8	HC	APLU	3													
CN		Piper					acid	l, 4-	[[4-	(2-b	utyn	vlox	y) ph	enyl	sul	fonv	1]-1	-[(4	-
		- F															• -	• • -	

methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me-C} = \text{C-CH}_2 - \text{O} \\ \text{O} \\ \text{O} \\ \text{O} \\ \text{O} \end{array}$$

5

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Ward 10 663042

L32 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:314178 HCAPLUS

DOCUMENT NUMBER: 134:326767

TITLE: Preparation of acetylenic α -amino acid-based

sulfonamide hydroxamic acid TACE inhibitors

INVENTOR(S): Levin, Jeremy I.; Chen, James M.; Cole, Derek C.; Du,

Mila T.; Laakso, Leif M.

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: U.S., 109 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6225311	B1	20010501	US 2000-492691	20000127 <
US 2003008849	A1	20030109	US 2000-748912	20001227 <
US 2003212049	A1	20031113	US 2003-376871	20030227 <
US 6716833	B2	20040406		
US 2004033988	A1	20040219	US 2003-377008	20030227
US 6812227	B2	20041102		
PRIORITY APPLN. INFO.:			US 1999-155249P	P 19990127
			US 2000-492691	A3 20000127
			US 2000-748912	B1 20001227

OTHER SOURCE(S): MARPAT 134:326767

Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO2, P(O)R10, where R10 = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R1 = H, aryl, alkyl, alkenyl, alkynyl; R2 = any group given for R1, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R1 and R2 may form a ring; R3 = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R1 and R3 may form a ring; R4, R5 = H, alkyl, CN, C.tplbond.CH; R6 = any group given for R1, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepared as inhibitors of TNF-α converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-methylbutyramide was prepared and showed IC50 = 7.4 nM for inhibition of TACE.

IT 287408-00-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of acetylenic α -amino acid-based sulfonamide hydroxamic acid TACE inhibitors)

RN 287408-00-8 HCAPLUS

CN 2-Aziridinecarboxylic acid, 1-[[4-(2-butynyloxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:824218 HCAPLUS

DOCUMENT NUMBER: 134:4752

TITLE: Preparation of hydroxamic acid derivatives as matrix

metalloprotease inhibitors

INVENTOR(S): Bedell, Louis J.; McDonald, Joseph J.; Barta, Thomas

E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos,

John N.; Mischke, Brent V.; Getman, Daniel P.;

Decrescenzo, Gary A.; Villamil, Clara I.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: PCT Int. Appl., 380 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 10

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. ______ ------- - - - -----WO 2000069819 **A1** 20001123 WO 2000-US6713 20000512 <--AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 2000-2373500 CA 2373500 20001123 AA 20000512 <--20020206 EP 2000-931910 EP 1177173 A1 20000512 <--AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO BR 2000011291 Α 20020514 BR 2000-11291 20000512 <--JP 2002544257 T2 20021224 JP 2000-618236 20000512 <--NZ 515197 Α 20040326 NZ 2000-515197 20000512

ZA 2001009007 A 20030131 ZA 2001-9007 20011031 <-PRIORITY APPLN. INFO.: US 1999-310813 A 19990512
WO 2000-US6713 W 20000512

OTHER SOURCE(S): MARPAT 134:4752

GI

Title compds. [I; W = 5, 6 membered aromatic, heteroarom. ring; R = 5, 6 membered cyclohydrocarbyl, heterocyclo, aryl, heteroaryl; R5. R6 independently = hydrido, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxyl, cyano, alkoxy, haloalkyl, haloalkyloxy, hydroxyalkyl, etc; R20 = alkoxy, aryloxy, alkoxyamino, benzyloxyamino, etc] and pharmaceutically acceptable salts with inter alia inhibits matrix metalloprotease activity are disclosed and a treatment that comprises administering a contemplated sulfonyl aromatic or heteroarom. hydroxamic acid in an MMP enzyme-inhibiting effective amount to a host having a condition associated with pathol. matrix metalloprotease activity are claimed. Thus, the title compound II was prepared and MMP-2, MMP-3, MMP-8, MMP-13, and MT1-MMP inhibition activities were assayed.

II

IT 213012-59-0P 308385-44-6P 308385-45-7P 308385-63-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)

RN 213012-59-0 HCAPLUS

CN Benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N - & S \\ & & \\ O & & \\ C - NH-OH \\ & & \\ O & \\ \end{array}$$

RN 308385-44-6 HCAPLUS

CN Benzamide, N-hydroxy-2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 308385-45-7 HCAPLUS

CN Benzeneacetamide, N, α -dihydroxy- α -methyl-2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 308385-63-9 HCAPLUS

CN Benzamide, 2-[[4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)

IT 213012-83-0P 213012-84-1P 213012-85-2P

308386-04-1P 308386-05-2P 308386-06-3P

308386-07-4P 308386-08-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)

RN 213012-83-0 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 213012-84-1 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 213012-85-2 HCAPLUS

CN Benzamide, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

RN 308386-04-1 HCAPLUS

CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 308386-05-2 HCAPLUS

CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 308386-06-3 HCAPLUS

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)

RN 308386-07-4 HCAPLUS

CN Benzeneacetic acid, α -hydroxy- α -methyl-2-[(4-phenyl-1-piperidinyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 308386-08-5 HCAPLUS

CN Benzeneacetamide, α -hydroxy- α -methyl-2-[(4-phenyl-1-piperidinyl)sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

IT 308385-92-4P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);

Ward 10_663042

BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)

RN 308385-92-4 HCAPLUS

CN Benzamide, 2-[(4-phenyl-1-piperidinyl)sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

IT 308385-98-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)

RN 308385-98-0 HCAPLUS

CN Benzamide, 2,3-dimethoxy-N-[(tetrahydro-2H-pyran-2-yl)oxy]-6-[[4-[4-(trifluoromethyl)phenyl]-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

3

ACCESSION NUMBER:

2000:535116 HCAPLUS

DOCUMENT NUMBER:

133:150472

TITLE:

Preparation of alkynyloxyphenylsulfonylmethylpiperidin

ehydroxamic acids and related compounds as inhibitors of matrix metalloproteinase and

TNF- α converting enzyme (TACE).

INVENTOR(S):

Levin, Jeremy Ian; Venkatesan, Aranapakam Mudumbai; Chen, James Ming; Zask, Arie; Sandanayaka, Vincent

Premarana; Du, Mila Ti; Baker, Jannie Lea

PATENT ASSIGNEE(S):

American Cyanamid Company, USA

SOURCE:

PCT Int. Appl., 136 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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PATENT NO.
                          KIND
                                 DATE
                                              APPLICATION NO.
                                                                      DATE
                          ----
     WO 2000044723
                          A1
                                 20000803
                                            WO 2000-US1864
                                                                      20000127 <--
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             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
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             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
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             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2356313
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                                             CA 2000-2356313
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                                                                      20000127 <--
     EP 1147085
                                              EP 2000-904569
                           Α1
                                 20011024
                                                                      20000127 <--
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                                                                      20010726 <--
PRIORITY APPLN. INFO.:
                                              US 1999-238038
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                                                                      19990127
                                              WO 2000-US1864
                                                                   W
                                                                      20000127
OTHER SOURCE(S):
                          MARPAT 133:150472
     R1C.tplbond.CCR2R3XYACR8R9(CR10R11)nCONR12OH (R1 = H, aryl, heteroaryl,
     alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl; R2, R3 = H, alkyl,
     cyano, CCH; R8-R11 = H, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl,
     alkyl, alkenyl, alkynyl; 1 of R8R9, R9R10, or R10R11 = atoms to form a
     cycloalkyl ring or a cycloheteroalkyl ring; R12 = H, aryl, heteroaryl,
     cycloalkyl, cycloheteroalkyl, alkyl; A, X = O, S, SO, SO2, NR7, CH2; R7 = H, aryl, aralkyl, heteroaryl, heteroaralkyl, etc.; Y = aryl, heteroaryl; A
     and X are not bonded to adjacent atoms of Y; n = 0-2), were prepared Thus,
     1-acetyl-4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-4-
     piperidinecarboxamide (preparation in several steps from Et isonipecotate
     given) inhibited TACE with IC50 = 4.8 nM.
IT
     287201-30-3P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and
        related compds. as inhibitors of matrix metalloproteinase and
        TNF-\alpha converting enzyme (TACE))
RN
     287201-30-3 HCAPLUS
CN
     4-Piperidinecarboxamide, 4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-
```

hydroxy-1-[(1-methyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

$$O-CH_2-C \equiv C-Me$$

IT 287202-66-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and related compds. as **inhibitors** of matrix metalloproteinase and $TNF-\alpha$ converting **enzyme** (TACE))

RN 287202-66-8 HCAPLUS

CN 4-Piperidinecarboxylic acid, 4-[[4-(2-butynyloxy)phenyl]sulfonyl]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:535102 HCAPLUS

DOCUMENT NUMBER: 133:150908

TITLE: Preparation of acetylenic α -amino acid-based

חאידים

sulfonamide hydroxamic acid TACE inhibitors

INVENTOR(S): Levin, Jeremy Ian; Chen, James Ming; Cole, Derek Cecil

ADDITONTON NO

DATE

PATENT ASSIGNEE(S): American Cyanamid Company, USA

KIMD

SOURCE: PCT Int. Appl., 293 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	TENT NO.	KIND	DATE	APPLICATION NO.	DATE			
	2000044709 2000044709	A3	20001221	WO 2000-US1981				
	CZ, DE, IN, IS, MD, MG, SK, SL, BY, KG, RW: GH, GM,	DK, DM, E JP, KE, K MK, MN, M TJ, TM, T KZ, MD, R KE, LS, M	E, ES, FI, G, KP, KR, W, MX, NO, R, TT, TZ, U, TJ, TM W, SD, SL,	BB, BG, BR, BY, CA, CH GB, GD, GE, GH, GM, HR KZ, LC, LK, LR, LS, LT NZ, PL, PT, RO, RU, SD UA, UG, UZ, VN, YU, ZA SZ, TZ, UG, ZW, AT, BE IT, LU, MC, NL, PT, SE	, HU, ID, IL, , LU, LV, MA, , SE, SG, SI, , ZW, AM, AZ,			
				MR, NE, SN, TD, TG	, , ,,,			
CA	2356299		20000803	CA 2000-2356299	20000127 <			
EP	1144368	A2	20011017	EP 2000-905750	20000127 <			
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BR	2000007752	A	20011204	BR 2000-7752	20000127 <			
	200102132							
JP	2002535382	T 2	20021022	JP 2000-595966	20000127 <			
AU	766717	B2	20031023					
NZ	511928	Α	20031128	NZ 2000-511928	20000127 <			
TW	593247	В	20040621	TW 2000-89101287	20000127			
AT	271035	E	20040715	AT 2000-905750	20000127			
PT	1144368	T	20040930	PT 2000-905750	20000127			
ES	2225089	Т3	20050316	ES 2000-905750 ·	20000127			
ZA	2001004326	Α	20020826					
NO	2001003674		20010924					
BG	105738	Α	20020531	BG 2001-105738	20010726 <			
	1038735	A1	20050107	HK 2002-100184	20020110			
PRIORIT	Y APPLN. INFO	.:		US 1999-238255 WO 2000-US1981				
OMITTED OF	NIDGE (C)	MADDA	m 122 1500					

OTHER SOURCE(S): MARPAT 133:150908

Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO2, P(O)R10, where R10 = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R1 = H, aryl, alkyl, alkenyl, alkynyl; R2 = any group given for R1, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R1 and R2 may form a ring; R3 = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R1 and R3 may form a ring; R4, R5 = H, alkyl, CN, C.tplbond.CH; R6 = any group given for R1, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepared as inhibitors of TNF-α converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-

Ward 10 663042

methylbutyramide was prepared and showed IC50 = 7.4 nM for inhibition of TACE.

IT 287408-00-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of acetylenic α -amino acid-based sulfonamide hydroxamic acid TACE inhibitors)
287408-00-8 HCAPLUS

RN

2-Aziridinecarboxylic acid, 1-[[4-(2-butynyloxy)phenyl]sulfonyl]-, methyl CN ester (9CI) (CA INDEX NAME)

L32 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1999:819347 HCAPLUS

DOCUMENT NUMBER:

132:64103

TITLE:

Preparation of amidino and guanidino azetidinone

compounds as tryptase inhibitors

INVENTOR(S):

Bisacchi, Gregory; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven;

Kronenthal, David R.; Randazzo, Michael E.; Xu, Zhongmin; Shi, Zhongping; Schwinden, Mark D.

PATENT ASSIGNEE(S):

Bristol-Myers Squibb Co., USA

SOURCE:

PCT Int. Appl., 326 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO	. DATE	
WO 9967215		A1	19991229	WO 1999-US1381	l 19990618 <
W: AL	AM, A	, AU, AZ	, BA, BB,	BG, BR, BY, CA, Cl	i, CN, CU, CZ, DE,
DK	EE, ES	, FI, GB	, GD, GE,	GH, GM, HR, HU, II	O, IL, IN, IS, JP,
KE	KG, KI	, KR, KZ	, LC, LK,	LR, LS, LT, LU, L	/, MD, MG, MK, MN,
MW	MX, NO	, NZ, PL	, PT, RO,	RU, SD, SE, SG, S	[, SK, SL, TJ, TM,
TR	TT, UA	, UG, UZ	, VN, YU,	ZA, ZW, AM, AZ, B	Y, KG, KZ, MD, RU,
TJ	TM				
RW: GH	GM, KI	, LS, MW	, SD, SL,	SZ, UG, ZW, AT, B	E, CH, CY, DE, DK,
ES	FI, FI	, GB, GR	, IE, IT,	LU, MC, NL, PT, S	E, BF, BJ, CF, CG,
CI	CM, G	, GN, GW	, ML, MR,	NE, SN, TD, TG	
CA 2336003		AA	19991229	CA 1999-233600	3 19990618 <
AU 9946950		A1	20000110	AU 1999-46950	19990618 <

AU	752320	B2	2	002	0912																
EP	1089973			A1	2	001	0411		EP 1999-930402								19990618 <				
•	R: AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	₹, :	ΙT,	LI,	LU	, NL	, SE	, MC	PT,	,			
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									WO	199	99-1	US13	811		W	19990	618				
OTHER SO	URCE(S):	:		MARP	AT 1	32:	6410	3													
			. :	MARP	AT 1	32:	6410								_						

GI

AB Novel β -lactam compds., e.g. of formula I [R - CO2H, CONH-alkyl, etc.; X = CONH(CH2)2NHCO2alkyl, etc.; n = 1-6;], are prepared as inhibitors of in vivo enzyme systems including tryptase, thrombin, trypsin, factor Xa, factor VIIa, and urokinase-type plasminogen activator (no data). The tryptase activity makes the title compds. useful as antiinflammatory agents in the treatment of chronic asthma and allergic Thus, II was prepared from (4S)-N-(tertrhinitis. butyldimethylsilyl)azetidin-2-one-4-carboxylic acid, tert-butyl-1piperazine carboxylate and tert-Bu isocyanate.

IT 253174-33-3P 253174-35-5P 253174-36-6P 253174-39-9P 253174-40-2P 253174-53-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amidino and guanidino azetidinone compds. as tryptase inhibitors)

RN253174-33-3 HCAPLUS

2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-[[4-(1,1-CN dimethylethyl)phenyl]sulfonyl]-4,4-dimethyl-, monohydrochloride (9CI) INDEX NAME)

● HCl

RN 253174-35-5 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 253174-34-4 CMF C15 H22 N4 O3 S

$$\begin{array}{c|c} O & \\ Me & O = S-Ph \\ Me & NH \\ \parallel \\ H_2N-C-NH-(CH_2)_3 & O \end{array}$$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 253174-36-6 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

HCl

RN 253174-39-9 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-([1,1'-biphenyl]-4-ylsulfonyl)-4,4-dimethyl-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ H_2N & & \\ & & \\ NH & & \\ \end{array}$$

● HCl

RN 253174-40-2 HCAPLUS

CN Piperidine, 1-[4-[[(3R)-3-[3-[(aminoiminomethyl)amino]propyl]-2,2-dimethyl-4-oxo-1-azetidinyl]sulfonyl]benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 253174-53-7 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 253174-52-6 CMF C15 H22 N4 O3 S

Absolute stereochemistry. Rotation (-).

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 253176-09-9P 253176-75-9P 253176-76-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidino and guanidino azetidinone compds. as tryptase inhibitors)

RN 253176-09-9 HCAPLUS

CN 2-Azetidinecarboxylic acid, 1-([1,1'-biphenyl]-4-ylsulfonyl)-3-[3-[[bis[[(phenylmethoxy)carbonyl]amino]methylene]amino]propyl]-4-oxo-, phenylmethyl ester, (2S,3R)- (9CI) (CA INDEX NAME)

RN 253176-75-9 HCAPLUS

CN Carbamic acid, [[3-[(3R)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 253176-76-0 HCAPLUS

CN Carbamic acid, [[3-[(3S)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

2

ACCESSION NUMBER:

1999:672748 HCAPLUS

DOCUMENT NUMBER:

131:299363

TITLE:

Substituted pyrrolidine hydroxamate metalloprotease

inhibitors

INVENTOR(S):

Cheng, Menyan; Natchus, Michael George; De, Biswanath;

Almstead, Neil Gregory; Taiwo, Yetunde Olabisi; Pikul, Stanislaw

PATENT ASSIGNEE(S):

The Procter & Gamble Company, USA

SOURCE:

PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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APPLICATION NO.
                                                                                           DATE
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                                 KIND
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                                           19991021 WO 1999-US7826 19990409 <--
      WO 9952868
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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      AU 9935522
                                   A1
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                                            20001219 BR 1999-9620
20010207 EP 1999-917387
      BR 9909620
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      EP 1073635
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      NZ 507076
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NO 2000005196
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                                                                                             20001016 <--
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                                                                                  P 19980414
W 19990409
                                                             US 1998-81667P
PRIORITY APPLN. INFO.:
                                                             WO 1999-US7826
                                MARPAT 131:299363
```

OTHER SOURCE(S):

GI

Title compds. I [R1 = OH, alkoxy, (un) substituted NHOH; X = SO2, CO, CO2, AB (un) substituted CONH, POH; R2 = H, alkyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aryloxy, heteroaryloxy; Z = (un)substituted NH, CH2; m, n = 0-4] are potent inhibitors of metalloproteases (no data) and are effective in treating conditions characterized by excess activity of these enzymes. Thus, cis-hydroxy-D-proline was treated with 4-MeOC6H4SO2Cl, esterified, oxidized to the ketone, and treated with NH2OK to give I [R1 = NHOH, XR2 = SO2C6H4OMe-4, Z = NOH, m, n

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203934-42-3P 203934-63-8P 203934-64-9P
IT
     203994-80-3P 204072-55-9P 247058-60-2P
     247058-61-3P 247058-62-4P 247058-63-5P
     247058-64-6P 247058-65-7P 247058-67-9P
     247058-68-0P 247058-70-4P 247058-71-5P
     247058-72-6P 247058-73-7P 247058-74-8P
     247058-75-9P 247058-76-0P 247058-77-1P
     247058-78-2P 247058-79-3P 247058-80-6P
     247058-81-7P 247058-82-8P
```

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of arylsulfonylpyrrolidinecarboxylates as metalloprotease inhibitors)

RN 203934-42-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 203934-63-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 203934-64-9 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 203994-80-3 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-55-9 HCAPLUS
CN D-Proline, 4-hydroxy-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4R)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 247058-60-2 HCAPLUS CN D-Proline, 4-(methoxyimino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry unknown.

RN 247058-61-3 HCAPLUS

CN D-Proline, 1-[(4-ethoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 247058-62-4 HCAPLUS

CN D-Proline, 1-[(4-ethoxyphenyl)sulfonyl]-4-(methoxyimino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-63-5 HCAPLUS

CN D-Proline, 4-oxo-1-[(4-propoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 247058-64-6 HCAPLUS

CN D-Proline, 4-(methoxyimino)-1-[(4-propoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-65-7 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(methoxyimino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-67-9 HCAPLUS

CN D-Proline, 4-oxo-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 247058-68-0 HCAPLUS

CN D-Proline, 4-(methoxyimino)-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-70-4 HCAPLUS

CN D-Proline, 1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-4-hydroxy-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 247058-71-5 HCAPLUS

CN D-Proline, 1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 247058-72-6 HCAPLUS

CN D-Proline, 1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-4-(methoxyimino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-73-7 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 247058-74-8 HCAPLUS

CN D-Proline, 4-oxo-1-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 247058-75-9 HCAPLUS

CN D-Proline, 4-(methoxyimino)-1-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-,
 methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-76-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(ethoxyimino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-77-1 HCAPLUS

CN D-Proline, 4-[(1,1-dimethylethoxy)imino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry unknown.

RN 247058-78-2 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(1,1-dimethylethoxy)imino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-79-3 HCAPLUS

CN D-Proline, 4-[(1,1-dimethylethoxy)imino]-1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-80-6 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1-piperidinylimino)-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry unknown.

RN 247058-81-7 HCAPLUS

Absolute stereochemistry.

Double bond geometry unknown.

RN 247058-82-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-methylene-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1999:576925 HCAPLUS

DOCUMENT NUMBER:

131:214289

Ward 10_663042

Preparation of oxadiazolyl piperidine derivatives as TITLE:

rotamase enzyme inhibitors

Bull, David John; MaGuire, Robert John; Palmer, INVENTOR(S):

Michael John; Wythes, Martin James

PATENT ASSIGNEE(S):

Pfizer Inc., USA; Pfizer Ltd. PCT Int. Appl., 237 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

GΙ

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

					KIND DATE			APPLICATION NO.						DATE			
	9945006							WO 1999-IB259									
	W:	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	ВG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
							GE,										
		KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
							RU,										
							YU,										
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							ΙT,					SE,	BF,	ΒJ,	CF,	CG,	CI,
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CA	2322442			AA 19990910			CA 1999-2322442					19990215 <					
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PT	PT 1060178				T 20031231												
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PRIORIT	Y APP	LN.	INFO	.:							.998-					9980	
										WO 1	.999-	IB25	9		W 1	9990	215
OTHER SOURCE(S):					MARPAT 131:2142			39									

Oxadiazolyl piperidine derivs. and analogs (I) [R1 = 5- or 6-membered heteroaryl (un)substituted ring containing 1-4 N, or 1 S or O and/or 1-2 N $_{\odot}$ AΒ atoms; R2 = H, (un) substituted Ph, (un) substituted C3-7 cycloalkyl, or 5-, 6-, or 7-membered (un) substituted heterocycle; A = C3-5 alkylene; W =

II

Ward 10_663042

direct link, C1-6 alkylene, or C2-6 alkenylene; X = direct link, C1-6 alkylene, or alkylene-Z-alkylene; Y = SO2, CO, (un)substituted CO-NH, CO-CO, CH2-CO, CS-CO, CO-CS, or CO-CH(OH); Z = O, S, (un)substituted CH2-NH, CH(aryl), NH, NH-CO2, CO-NH, or NH-CO) were prepared as rotamase enzyme inhibitors, particularly FKBP-12 and FKBP-52 inhibitors, to moderate neuronal regeneration and outgrowth. Thus, ethyldiisopropylamine was added to a mixture of 5-benzyl-3-[(2S)-2piperidyl]-1,2,4-oxadiazole hydrochloride (preparation given) and 1H-benzo[d]imidazole-2-sulfonyl chloride (preparation given) in CH2Cl2 and the mixture was stirred for 18 h to yield 1H-benzo[d]imidazol-2-yl [(2S)-2-(5-benzyl-1,2,4-oxadiazol-3-yl)-1-piperidyl] sulfone (II). compds. of the invention were tested for in vitro inhibitory activity against the FKBP-12 enzyme in a coupled colorimetric PPlase assay, and exhibited IC50 values in the range of 81 nm to 2010 nm. One compound was assayed for inhibitory activity against the FKBP-52 enzyme and gave a Ki value of 685. The compds. are claimed to be useful in treating neurol. disorders arising from neurodegenerative diseases and nerve damage.

IT 242459-55-8P 242459-66-1P 242459-72-9P 242459-74-1P 242459-78-5P 242459-94-5P 242459-95-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of oxadiazolyl piperidine derivs. as rotamase enzyme inhibitors for treatment of neurol. disorders arising from neurodegenerative diseases and nerve damage)

RN 242459-55-8 HCAPLUS

CN

Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[(4-formylphenoxy)methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)

RN 242459-66-1 HCAPLUS

CN 2-Piperidinecarboximidic acid, 1-[(4-fluorophenyl)sulfonyl]-, ethyl ester, (2S)- (9CI) (CA INDEX NAME)

RN 242459-72-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(4-fluorophenyl)sulfonyl]-, methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 242459-74-1 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(4-fluorophenyl)sulfonyl]-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-78-5 HCAPLUS

CN Carbamic acid, [2-[4-[[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-1,2,4-oxadiazol-5-yl]methyl]phenoxy]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 242459-94-5 HCAPLUS

CN Piperidine, 2-[5-(cyclohexylideneamino)-1,3,4-oxadiazol-2-yl]-1-[(4-fluorophenyl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 242459-95-6 HCAPLUS

CN Carbamic acid, [[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-1,2,4-oxadiazol-5-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

IT 242458-82-8P 242458-83-9P 242458-98-6P 242458-99-7P 242459-04-7P 242459-24-1P 242459-27-4P 242459-38-7P 242459-40-1P

242459-41-2P 242459-42-3P 242459-43-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of oxadiazolyl piperidine derivs. as rotamase enzyme inhibitors for treatment of neurol. disorders arising from neurodegenerative diseases and nerve damage)

RN

242458-82-8 HCAPLUS
Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-[(1,3-dihydro-1,3-CN dioxo-2H-isoindol-2-yl) methyl] phenoxy] methyl] -1,2,4-oxadiazol-3-yl] -, (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN

242458-83-9 HCAPLUS
Piperidine, 2-[5-[[4-(aminomethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-1-CN (1H-benzimidazol-2-ylsulfonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

242458-98-6 HCAPLUS RN

Carbamic acid, [2-[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-CN 1,2,4-oxadiazol-5-yl]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 242458-99-7 HCAPLUS

CN Piperidine, 2-[5-(2-aminoethyl)-1,2,4-oxadiazol-3-yl]-1-(1H-benzimidazol-2-ylsulfonyl)- (9CI) (CA INDEX NAME)

RN. 242459-04-7 HCAPLUS

CN Piperidine, 2-(5-amino-1,3,4-oxadiazol-2-yl)-1-[(4-fluorophenyl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-24-1 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[(4-piperidinyloxy)methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

RN 242459-27-4 HCAPLUS

CN Piperidine, 1-[(5-bromo-1H-benzimidazol-2-yl)sulfonyl]-2-[5-[[4-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

 $\sim_{\mathtt{Br}}$

RN 242459-38-7 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-

(hydroxymethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)

RN 242459-40-1 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(1H-1,2,4-triazol-3-yl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 242459-41-2 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(1H-tetrazol-5-yl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-42-3 HCAPLUS

CN Piperidine, 2-[5-(aminomethyl)-1,2,4-oxadiazol-3-yl]-1-(1H-benzimidazol-2-

ylsulfonyl) - (9CI) (CA INDEX NAME)

RN 242459-43-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[3-[(2S)-1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-1,2,4-oxadiazol-5-yl]methoxy]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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242458-73-7P 242458-74-8P 242458-84-0P
IT
     242458-85-1P 242458-86-2P 242459-00-3P
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     242459-08-1P 242459-09-2P 242459-10-5P
     242459-11-6P 242459-12-7P 242459-13-8P
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     242459-17-2P 242459-18-3P 242459-19-4P
     242459-20-7P 242459-21-8P 242459-22-9P
     242459-23-0P 242459-25-2P 242459-26-3P
     242459-28-5P 242459-37-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of oxadiazolyl piperidine derivs. as rotamase enzyme
        inhibitors for treatment of neurol. disorders arising from
        neurodegenerative diseases and nerve damage)
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RN 242458-73-7 HCAPLUS CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-(phenylmethyl)-1,2,4oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242458-74-8 HCAPLUS

CN Piperidine, 1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 242458-84-0 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-[(dimethylamino)methyl]phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242458-85-1 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-(1-pyrrolidinylmethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)

RN 242458-86-2 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-[(methylamino)methyl]phenoxy]methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)

RN 242459-00-3 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[2-[(phenylmethyl)amino]ethyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)

RN 242459-01-4 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-1,3,4-thiadiazol-2-yl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-02-5 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[1-(phenylmethyl)-1H-1,2,4-triazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 242459-03-6 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[4-methyl-5-(phenylmethyl)-4H-1,2,4-triazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-05-8 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-[(phenylmethyl)amino]-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

242459-06-9 HCAPLUS
Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(3-methyl-5-isoxazolyl)-, (2S)-CN (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-07-0 HCAPLUS

Pyrrolidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-CNoxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

242459-08-1 HCAPLUS RN

Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-CNoxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

RN 242459-09-2 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-[[4-(hydroxymethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 242459-10-5 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-phenyl-1,2,4-oxadiazol-3-yl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-11-6 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-pyrazinyl-1,2,4-oxadiazol-3-yl)-, (2S)- (9CI) (CA INDEX NAME)

RN 242459-12-7 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-1,3,4-oxadiazol-2-yl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-13-8 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(phenylmethyl)-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-14-9 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(2-phenylethyl)-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

RN 242459-15-0 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[2-(phenylmethyl)-2H-tetrazol-5-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-16-1 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(2-methyl-2H-tetrazol-5-yl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-17-2 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-1H-1,2,4-triazol-3-yl)-, (2S)- (9CI) (CA INDEX NAME)

RN

242459-18-3 HCAPLUS
Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-2-thiazolyl)-, (2S)-CN (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

242459-19-4 HCAPLUS RN

Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(3-methyl-1,2,4-oxadiazol-5-yl)-CN, (2S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

242459-20-7 HCAPLUS RN

Piperidine, 2-[5-(cyclohexylamino)-1,3,4-oxadiazol-2-yl]-1-[(4-CN fluorophenyl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

RN 242459-21-8 HCAPLUS

CN Piperidine, 2-[5-[[4-(2-aminoethoxy)phenyl]methyl]-1,2,4-oxadiazol-3-yl]-1-(1H-benzimidazol-2-ylsulfonyl)- (9CI) (CA INDEX NAME)

RN 242459-22-9 HCAPLUS

CN Benzamide, N-[2-[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-1,2,4-oxadiazol-5-yl]ethyl]- (9CI) (CA INDEX NAME)

RN 242459-23-0 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[(phenylmethyl)amino]methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)

RN 242459-25-2 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[[1-(cyclopropylmethyl)-4-piperidinyl]oxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 242459-26-3 HCAPLUS

CN Piperidine, 1-[(5-bromo-1H-benzimidazol-2-yl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

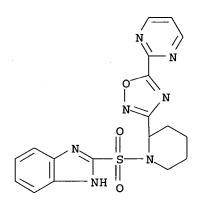
Absolute stereochemistry. Rotation (-).

RN 242459-28-5 HCAPLUS

CN Piperidine, 2-[5-[[4-(aminomethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-1-[(5-bromo-1H-benzimidazol-2-yl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

RN 242459-37-6 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-(2-pyrimidinyl)-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:9831 HCAPLUS

DOCUMENT NUMBER: 130:81407

TITLE: Novel tricyclic [benzocycloheptapyridine] sulfonamide

inhibitors of farnesyl-protein transferase

INVENTOR(S): Njoroge, F. George; Vibulbhan, Bancha; Taveras, Arthur

G.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.

PATENT ASSIGNEE(S): Schering Corporation, USA.

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND I	DATE	APPLICATION NO.	DATE
	71 1	10001222	WO 1000 UC11500	10000615
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PRIORITY APPLN. INFO.:
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                                             WO 1998-US11508
OTHER SOURCE(S):
                         MARPAT 130:81407
GI
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

- Novel compds. I [A = N or N(O); X = C, CH or N; X1, X2 = Cl, Br, iodo; X3, AB X4 = H, Br, iodo, Cl, F, provided that only one is H; R5-R8 = H, alkyl, aryl, (un) substituted carbamoyl; or R5R6 and/or R7R8 = 0 or S; R alkyl, aryl, aralkyl, heteroaryl, cycloalkyl, (un)substituted NH2], which are inhibitors of the enzyme farnesyl protein transferase (FPT), are disclosed. Pharmaceutical compns. containing I, methods of inhibiting Ras function with them, and methods for inhibiting abnormal cell growth (i.e., treating tumor cells) with them are also disclosed. Fourteen examples were prepared For instance, the starting material II [X3 = H] was converted to II [X3 = Cl] in 4 steps, and the latter was converted in multiple steps, ending with the sulfonylation of an N-unsubstituted piperidine derivative with MeSO2Cl in the presence of K2CO3, to give invention compound III. The latter inhibited Ras-CVLS farnesylation by rat brain FPT in vitro with IC50 of 0.0080 μM.
- IT 218801-06-0P 218801-07-1P 218801-08-2P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of benzocycloheptapyridine sulfonamide derivs. as farnesyl protein transferase inhibitors)

RN 218801-06-0 HCAPLUS

CN Piperidine, 4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 218801-07-1 HCAPLUS

CN Piperidine, 4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 218801-08-2 HCAPLUS

CN Piperidine, 4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-[[5-(3-isoxazolyl)-2-thienyl]sulfonyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

6

ACCESSION NUMBER:

1998:653554 HCAPLUS

DOCUMENT NUMBER:

129:290060

TITLE:

Certain alpha-azacycloalkyl substituted

arylsulfonamido acetohydroxamic acids, useful as

inhibitors of matrix-degrading

metalloproteinases and TNF- α converting

enzyme

INVENTOR(S):

Nantermet, Philippe G.; Parker, David T.; Macpherson,

Lawrence J.

PATENT ASSIGNEE(S):

Novartis Corporation, USA

SOURCE:

U.S., 19 pp., Cont.-in-part of U.S. 5,646,167. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	Ι	DATE		
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US 5817822	Α	19981006	US 1997-787730	1	19970124 <		
US 5506242	Α	19960409	US 1994-265296	1	19940624 <		
US 5552419	Α	19960903	US 1994-333676	1	19941103 <		
US 5646167	Α	19970708	US 1995-475166	1	19950607 < - -		
PRIORITY APPLN. INFO.:			US 1994-265296	A2 1	19940624		
			US 1994-333676	A2 1	19941103		
			US 1995-475166	A2 1	19950607		
			US 1993-1136	A2 1	19930106		
			NZ 1993-250517	A :	19931220		

MARPAT 129:290060 OTHER SOURCE(S):

GI

AΒ The invention relates to α -(N-substituted pyrrolidinyl and piperidinyl) - α -(arylsulfonamido) acetohydroxamic acids I [R = acyl derived from a carboxylic, carbonic, or carbamic acid; or R = (lower alkyl, aryl-lower alkyl, or aryl)-sulfonyl, di-(aryl-lower alkyl or alkyl)-aminosulfonyl, or aryl-lower alkyl; Ar = carbocyclic aryl, heterocyclic aryl, or biaryl; R1 and R2 = H, alkyl, alkoxy, halo, OH, acyloxy, alkoxy-lower alkoxy, CF3, or cyano; or R1R2 = alkylenedioxy; m = 0 or 1; n = 1-5] and their pharmaceutically acceptable prodrugs and salts. Also disclosed are a process for the preparation of the compds., pharmaceutical compns. comprising them, and their use for therapeutic treatment or manufacture of a pharmaceutical composition Approx. 70 invention compds. and various starting materials and intermediates are described. For instance, benzyl 2-(R)-[(4-methoxybenzenesulfonyl)(4-picolyl)amino]-2-(4piperidinyl)acetate dihydrochloride (prepared in approx. 9 steps) was condensed at the piperidine N with 1-naphthaleneethanol and di(2-pyridyl) carbonate (phosgene equivalent), and the product underwent hydrogenolysis of the benzyl ester, amidation with tert-BuONH2, and removal of the tert-Bu group with dry HCl, to give title salt II.HCl. In a test for inhibition of production of soluble TNF- α by LPS-stimulated THP-1 cells in vitro, II.HCl had an IC50 of 0.7 μM . II.HCl also inhibited the in-vitro hydrolysis of substance P by stromelysin with an IC50 of approx. 15 nM. IT 214217-61-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of azacycloalkyl arylsulfonamido acetohydroxamic acids as **inhibitors** of matrix-degrading metalloproteinases and TNF- α converting **enzyme**)

RN 214217-61-5 HCAPLUS

CN

4-Piperidineacetic acid, α -[[(4-methoxyphenyl)sulfonyl](4-pyridinylmethyl)amino]-1-[(4-methylphenyl)sulfonyl]-, phenylmethyl ester, (α R)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

7

ACCESSION NUMBER:

1998:611997 HCAPLUS

DOCUMENT NUMBER:

129:260344

TITLE:

Preparation of sulfonyl divalent aryl or heteroaryl hydroxamic acid compounds as inhibitors of matrix

metalloprotease

INVENTOR (S):

Mcdonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.

PATENT ASSIGNEE(S):

SOURCE:

Monsanto Company, USA PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT 1	NO.			KIND DATE			APPLICATION NO.						DATE				
WO 9838859				A1 19980911				WO 1998-US4300						19980304 <				
											CZ,					HU,	ID,	
											LV,							
											US,							
					RU,			-										
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	
											SE,							
		-						TD,										
CA 2283275			AA 19980911				CA 1998-2283275						19980304 <					
								AU 1998-65424										
AU 750130			В2	B2 20020711														
EP	EP 973392			A1		20000126 EP 1998-911481 199							9980	304 <				
	EP 973392					2003												
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,									IE, FI	
BR	R 9808166			Α		2000	0516											
	NZ 337326					2001	0525											
JP 2001518081																		
CN	CN 1105114				В		2003	0409	CN 1998-804575									
AΤ	AT 254599				E			1215	AT 1998-911481									
PT	9733	92			T 20040430					PT 1998-911481					the state of the s			
ES	ES 2206903				T3 20040516				ES 1998-911481									
ES	ES 2209122				Т3			0616			.998-					9980		
US	US 2001020021					20010906 US 1999-230209 19							9990	624 <	-			
US 6380258				В2		2002	0430											

Ward 10_663042

NO 9904252	Α	19990902	NO	1999-4252		19990902	<
NO 315647	B1	20031006					
MX 9908156	Α	20000228	MX	1999-8156		19990903	<
US 2003191317	Al	20031009	US	2000-728408		20001201	<
US 6794511	B2	20040921					
US 2003073845	A1	20030417	US	2001-909227		20010719	<
US 6696449	B2	20040224					
US 2002103239	A1	20020801	US	2001-997552		20011129	<
US 6656954	B2	20031202					
US 2005075374	A1	20050407	US	2004-867391		20040614	
PRIORITY APPLN. INFO.	:		US	1997-35182P	P	19970304	
			WO	1998-US4300	W	19980304	
			US	1999-310813	B1	19990512	
			US	1999-230209	A2	19990624	
			US	2000-569034	A2	20000511	
			US	2000-728408	A2	20001201	

OTHER SOURCE(S):

MARPAT 129:260344

GI

$$\begin{array}{c|c} & \mathbb{R}^2 & \mathbb{R}^3 \\ \text{HONH} & & & & \\ \mathbb{Q} & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\$$

Sulfonyl divalent aromatic or heteroarom. ring hydroxamic acid compds. (I; m, AB n = 0 or 1 and m+n = 1; R1 = a substituent containing a 5- or 6-membered cyclohydrocarbyl, heterocyclyl, aryl, or heteroaryl radical bonded directly to the depicted SO2-group and having a length greater than about that of a hexyl group and less than about that of an eicosyl group; R1 defines a three-dimensional volume, when rotated about an axis drawn through the SO2-bonded 1-position and the center of 3,4-bond of a 5-membered ring radical, whose widest dimension in a direction transverse to the axis of rotation is about that of one furanyl ring to about that of two Ph rings; R2, R3 = hydrido, C1-4 hydrocarbyl, OH, or NH2 or R2 and R3 together with the depicted carbon atom to which they are bonded from a 6-membered heterocyclic ring containing O, S, or N heteroatom, said heteroatom being optionally substituted with one or two O atoms when sulfur and being optionally substituted with a moiety selected from the group consisting of a C1-4 hydrocarbyl, C3-6 cyclohydrocarbyl, C1-4 acylhydrocarbyl, and sulfonyl-C1-4 hydrocarbyl when nitrogen) that inter alia inhibits matrix metalloprotease activity are disclosed. Also disclosed is a treatment process that comprises administering a contemplated sulfonyl divalent aromatic or heteroarom. ring hydroxamic acid compound in an MMP enzyme-inhibiting effective amount to a host having a condition associated with pathol. matrix metalloprotease activity. Thus, 2-fluorobenzaldehyde was condensed with 4-phenoxybenzenethiol in the

Ward 10_663042

presence of K2CO3 under reflux for 20 h to give 2-(4-phenoxyphenylthio) benzaldehyde (II). Tetra-Et dimethylammoniomethylenediphosphonate was treated with NaH in THF and then condensed with II at ambient temperature for 4 h to give [2-(4-phenoxyphenylthio)phenyl]acetic acid which was oxidized with a mixture of 30% H2O2 and AcOH at 100° for 40 min to give [2-(4-phenoxyphenylsulfonyl)phenyl]acetic acid. The latter compound was condensed with O-tetrahydropyranylhydroxylamine using EDC in MeCN followed by treatment with p-MeC6H4SO3H in MeOH to give the title compound (III), which showed IC50 of 2, 900, and 0.3 nM against MMP-13, MMP-1, and MMP-2, resp.

IT 213012-59-0P RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sulfonyl divalent aryl or heteroaryl hydroxamic acid compds. as inhibitors of matrix metalloprotease)

RN 213012-59-0 HCAPLUS

CN Benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

IT 213012-83-0P 213012-84-1P 213012-85-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of sulfonyl divalent aryl or heteroaryl hydroxamic acid compds. as inhibitors of matrix metalloprotease)

RN 213012-83-0 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{Ph-} & \text{CH}_2 & & & \\ & & & & \\ \end{array}$$

RN 213012-84-1 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 213012-85-2 HCAPLUS

Benzamide, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-N-[(tetrahydro-2H-CN pyran-2-yl)oxy] - (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1998:251152 HCAPLUS

DOCUMENT NUMBER:

128:321926

TITLE: -

Preparation of aspartate ester inhibitors of

INVENTOR (S):

interleukin-1 β converting enzyme Albrecht, Hans P.; Allen, Hamish John; Brady, Kenneth Dale; Caprathe, Bradley William; Gilmore, John Lodge; Harter, William Glen; Hays, Sheryl Jeanne; Kostlan, Catherine Rose; Lunney, Elizabeth Ann; Para, Kimberly

Suzanne; et al.

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 179 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English .

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816502	A1	19980423	WO 1997-US18514	19971009 <
W: AL, AU	BA, BB, BG	B, BR, CA,	CN, CZ, EE, GE, HU, I	L, IS, JP, KR,
			MN, MX, NO, NZ, PL, R	
SL, TR	TT, UA, US	S, UZ, VN,	YU, AM, AZ, BY, KG, K	Z, MD, RU, TJ, TM
			ZW, AT, BE, CH, DE, D	
GB, GR	IE, IT, LU	J, MC, NL,	PT, SE, BF, BJ, CF, C	G, CI, CM, GA,
GN, ML	MR, NE, SN	I, TD, TG		
CA 2268098	AA	19980423	CA 1997-2268098	19971009 <
AU 9749023	A1	19980511	AU 1997-49023	19971009 <i>°</i> <
AU 738341	B2	20010913		

Ward 10 663042

EP 932598 R: AT, BE, CH, IE, SI, LT,			EP 1997-911715 B, GR, IT, LI, LU, NL,	19971009 < SE, MC, PT,
			DD 1007 10530	19971009 <
BR 9712530	Α	19991019	BR 1997-12530	
JP 2001506974	T2	20010529	JP 1998-518519	19971009 <
NO 9901677	A	19990609	NO 1999-1677	19990409 <
KR 2000049048	Α	20000725	KR 1999-703117	19990410 <
PRIORITY APPLN. INFO.:			US 1996-28322P	P 19961011
			WO 1997-US18514	W 19971009
OTHER SOURCE(S):	MARPAT	128:321926		

The present invention relates to compds. I [R1 = carboxy, acyl, amino acid AB residue, etc.; R2 = (CR2)n-X-R3; each R = independently H, C1-6 alkyl, OH; R3 = (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, cycloalkyl, etc; X = bond, O, S; n = 0-3; and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof] as inhibitors of interleukin-1β converting enzyme (ICE). This invention also relates to a method of treatment of stroke, inflammatory diseases, reperfusion injury, Alzheimer's disease, and shigellosis, and to a pharmaceutically acceptable composition that contains a compound that is an inhibitor of $interleukin-1\beta$ converting enzyme. Thus, substitution of Z-Asp(OCMe3)-CH2Br (Z = PhCH2O2C) with 1-naphthylacetic acid, followed by acidic deprotection, gave desired aspartate ester derivative II. II inhibited ICE with Ki = 0.460 μM and IC50 = 3.100 μM , and inhibited Ich-2 (caspase-4) with IC50 = 3.60 μM , as determined using in vitro assays. Related prepared compds. I (196 examples) were also tested for ICE inhibition (Ki values of 0.00008 to 76 μM and IC50 values of 0.0013 to 32 μM), and Ich-2 inhibition (IC50 = 0.021 to 76 μ M).

IT 206863-33-4P

GΙ

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aspartate ester inhibitors of interleukin-1 β converting enzyme)

RN 206863-33-4 HCAPLUS

CN L-Proline, 1-[(4-methylphenyl)sulfonyl]-5-oxo-, 4-carboxy-2-oxo-3-[[(phenylmethoxy)carbonyl]amino]butyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1998:146700 HCAPLUS

DOCUMENT NUMBER:

128:213393

TITLE: INVENTOR(S): Method of using neurotrophic sulfonamide compounds Hamilton, Gregory S.; Li, Jia-he; Steiner, Joseph P. GPI NIL Holdings, Inc., USA

PATENT ASSIGNEE(S): GPI NIL Holdings,

SOURCE:

U.S., 14 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT :						ATE		1	APPL	ICAT	ION I	NO.		D	ATE		
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US	5721	256			Α	1	.998	0224	1	US 1	997-	7994	07		1	9970:	212	<
ZA	9800	824			Α	1	.998	1030		ZA 1	998-	824			1	9980:	202	<
CA	2280				AA	1	.998	0820	(CA 1	998-	2280	742		1	9980:	211	<
WO	9835	675			A1	1	998	0820	1	WO 1	998-1	US22	15		1:	9980:	211	<
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						GB,												
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OTHER SOURCE(S):

MARPAT 128:213393

GI

$$\begin{array}{c|c} & & & \\ & & & \\ N & & \\ N & & \\ Ph-CH_2-SO_2 & & \\ \end{array}$$

AB Low-mol.-weight sulfonamides, e.g. I, having an affinity for FKBP-type immunophilins and thus inhibitors of the enzyme activity associated with immunophilin proteins, particularly peptidyl-prolyl isomerase (rotamase), are useful for the treatment of neurol. disorders including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. An example was given for the preparation of I.

IT 204332-48-9 204332-49-0 204332-50-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rotamase-inhibiting sulfonamides for treatment of neurol. disorders)

RN 204332-48-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(phenylsulfonyl)-, 4-phenyl-1-(3-phenylpropyl)butyl ester (9CI) (CA INDEX NAME)

RN 204332-49-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[(4-methylphenyl)sulfonyl]-, 4-phenylbutyl ester (9CI) (CA INDEX NAME)

RN 204332-50-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(phenylsulfonyl)-, 4-phenylbutyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1998:112229 HCAPLUS

DOCUMENT NUMBER:

128:192667

TITLE:

Preparation of substituted aromatic compounds as

inhibitors of tumor necrosis factor and cyclic AMP

phosphodiesterase

INVENTOR(S):

He, Wei; Hulme, Christopher; Huang, Fu-chih; Djuric, Stevan W.; Moriarty, Kevin; Labaudiniere, Richard

PATENT ASSIGNEE(S):

Rhone-Poulenc Rorer Pharmaceuticals Inc., USA; He, Wei; Hulme, Christopher; Huang, Fu-Chih; Djuric, Stevan W.; Moriarty, Kevin; Labaudiniere, Richard

PCT Int. Appl., 154 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

GI

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	TENT	NO.			KINI)]	DATE		1	APPL	ICAT:	ION I	NO.		D	ATE		
					-,										-			
WO	9805	327			A1		1998	0212	1	WO 1:	997-1	US13:	343		1:	9970'	722 <	-
	W:	AL,	AM,	AT,	AU,	AZ,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,	
		ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LS,	
		LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	
		SE,	SG,	SI,	SK,	ТJ,	TM,	TR,	TT,	UA,	ŪĠ,	US,	UΖ,	VN,	AM,	ΑZ,	BY,	
		KG,	ΚZ,	MD,	RU,	TJ,	TM											
	RW:	GH,	ΚE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	
		GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	
		GN,	ML,	MR,	NE,	SN,	TD,	TG										
AU	9738	990			A1		1998	0225		AU 1	997-	3899	0		1:	9970	722 <	-
PRIORITY	Y APP	LN.	INFO	. :					1	US 1	996-:	2316	5 P	1	P 1:	9960	305	
									1	WO 1	9971	US13	343	1	W 1:	9970	722	
OTHER SO	OURCE	(S):			MARI	ТАЧ	128:	1926	67									

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention is directed to compound of formula [I; ring A = Q10, Q11; Ar1 = Q12, Q13, Q14; ring Ar2 = (un)substituted fused Ph or fused monocyclic heteroaryl; R = (un)substituted alkyl, aralkyl, or heteroaralkyl, arylsulfonyl, heteroarylsulfonyl, etc.; R1 = carboxyalkyl, alkoxycarbonylalkyl, N-(un)substituted carbamoylalkyl, cyanoalkyl,

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(un) substituted aralkyl or heteroaralkyl; R2 = (un) substituted lower alkyl; R3 = (un) substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, or oxaaliph., (un) substituted or optionally oxidized cyclothioalkyl or cyclothioalkenyl; R4, R6 = H, (un)substituted lower alkyl; R5 = (un) substituted alkyl, alkoxy, cycloalkyl, or heterocyclyl, alkoxycarbonyl, cyano, (un) substituted carbamoyl, (un) substituted aryl or heteroaryl, or CO2H where m is other than 0; R7 = H, alkoxy, (un) substituted cycloalkyl, cycloalkenyl, cycloalkoxy, cycloalkenyloxy, aryl, heteroaryl, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, alkylthio, or alkylsulfinyl, etc.; Q1, Q2 = CH2, O-(un)substituted CHOH, CO; Q3, Q4, Q5, Q9 = N, optionally halo-substituted CH; Q6 = N, CH; Q7-C-Q8 = N-(un)saturated NHCH:N, O-CH:CH, CH:CH-O, O-CH2CH2, CH2CH2O; Z', Z'' = H or Z'Z'' = O or S; Z1, Z2 = direct bond, O, S; Z3 = SO2, direct bond; Z4 = direct bond, O, S, NH; Z5 = direct bond, (un)substituted lower alkenyl; m, n = 0, 1; p = 1-3; q = 0-5] or hydrate, solvate, N-oxide, or prodrug thereof or a pharmaceutically acceptable salt thereof are. They are especially useful for inhibiting the production or physiol. effects of tumor necrosis factor (TNF) and inhibit cAMP phosphodiesterase and are useful for the treatment of disease states associated with abnormally high physiol. levels of cytokines such as TNF or those associated with pathol. (e.g. asthma as bronchodilators or inflammation) conditions that are modulated by inhibiting enzymes such as cAMP phosphodiesterase (no data). In particular, they are used for treating a disease state capable of being modulated by inhibiting TNF, e.g., joint inflammation, arthritis, rheumatoid arthritis, rheumatoid spondylitis and osteoarthritis, sepsis, septic shock, gram neg. sepsis, toxic shock syndrome, acute respiratory distress syndrome, asthma, bone resorption diseases, reperfusion injury, graft vs. host reaction, allograft rejection malaria, myalgias, HIV, AIDS, cachexia, Crohn's disease, ulcerative colitis, pyresis, systemic lupus erythematosus, multiple sclerosis, type I diabetes mellitus, psoriasis, Behcet's disease, anaphylactoid purpura nephritis, chronic glomerulonephritis, inflammatory bowel disease, and leukemia. They are also used for treating a pathol. condition associated with a function of cAMP phosphodiesterase, eosinophil accumulation or function of the eosinophil, e.g., asthma, atopic dermatitis, urticaria, allergic rhinitis, psoriasis, rheumatic arthritis, ulcerative colitis, Crohn's disease, adult respiratory distress syndrome, diabetes insipidus, keratosis, dermatitis, cerebral senility, multiinfarct dementia, senile dementia, memory impairment associated with Parkinson's disease, cardiac arrest, stroke, and intermittent claudication. present invention is also directed to their pharmaceutical use, pharmaceutical compns. containing the compds., and methods of their preparation Thus, 2-(3-cyclopentyloxy-4-methoxyphenyl)-5-hydroxymethyl-2-(4pyridylmethyl)indan-1,3-dione was treated with NaH in THF, tosylated by tosyl chloride at 0° to room temperature for 2 h, and then condensed with 1-methylpiperazine in the K2CO3 in acetone at room temperature for 4 days the presence of K2CO3 in acetone to give the title compound, piperazinylmethylpyridylmethylindandione derivative (II).

IT 203441-35-4P

CN

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted aromatic compds. as **inhibitors** of tumor necrosis factor and cAMP phosphodiesterase)

RN 203441-35-4 HCAPLUS

2-Pyrrolidinone, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[(4-methylphenyl)sulfonyl]-3-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:132788 HCAPLUS

DOCUMENT NUMBER: 126:141390

TITLE: Primer extension assays for detection of nucleases

producing single-stranded nucleic acids and the

screening of inhibitors

INVENTOR(S): Cole, James L.; Kuo, Lawrence C.; Olsen, David B.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT 1	. O <i>l</i>			KINI)	DATE		AP:	PLICAT	I NOI	NO.		D	ATE		
	. .					-											
WC	96409	994			A1		1996	1219	WO	1996-	US83	30		19	99606	03	<
	W:	CA,	JP,	US													
	RW:	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR, G	B, GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE
C	22226	688			AA		1996	1219	CA	1996-	22226	688		19	9606	03	< - -
EI	83394	45	•		A1		1998	0408	EP	1996-	9206	11		19	99606	03	<
EI	83394	45			B1		2002	0130									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB, G	R, IT,	LI,	LU,	NL,	SE,	PT,	ΙE,	FΙ
JI	1150	5607			T2		1999	0615	JP	1996-	50096	64		19	9606	03	<
ΑT	2126	76			E		2002	0215	AT	1996-	9206	11		19	9606	03	<
ES	21708	861			Т3		2002	0816	ES	1996-	9206	11		19	9606	03	<
US	61000	028			Α		2000	8080	US	1998-	97313	39		19	99807	31	<
PRIORIT	Y APPI	LN.	INFO	. :					US	1995-	48776	50	1	A 19	9506	07	
									WO	1996-	US833	30	V	V 19	9606	03	

AB An assay for enzymes that act on substrates to produce a single-stranded oligonucleotide product has been developed. The method uses DNA polymerase-catalyzed extension of the oligonucleotide cleavage product using labeled nucleotides and a DNA template containing a 3' region complementary to the oligonucleotide product joined to a 5' region

Ward 10 663042

consisting of repeated nucleotide residues. The DNA polymerase extension assay does not involve gel electrophoretic separation and is amenable to high volume screening of potential **inhibitors**. Other key features of the assay are that it monitors the substrate cleavage reaction only at the correct position in the sequence, thereby discriminating against nonspecific cleavage products, and that it is sensitive enough to detect 200 amol of product.

IT 186460-35-5

CN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of influenza virus endonuclease by; primer extension assays for detection of nucleases producing single-stranded nucleic acids and screening of inhibitors)

RN 186460-35-5 HCAPLUS

3-Piperidinebutanoic acid, 3-[(4-chlorophenyl)methyl]- α , γ -dioxo-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

L32 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:559909 HCAPLUS

DOCUMENT NUMBER: 119:159909

TITLE: Aromatic sulfonamide derivative inhibitors

of calcium-dependent enzymes and

phospholipase A2

INVENTOR(S):
Dumont, Raymond

PATENT ASSIGNEE(S): Pharno-Wedropharm G.m.b.H., Germany

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATE	ENT NO.		KINI	D DATE	APPLICATION NO.	DATE
WO 9						19910905 <
		-			DE, DK, ES, FI, GB, HG PL, RO, SD, SE, SU, US	
	-			DK, ES, FR, GN, ML, MR,	GB, GR, IT, LU, NL, SI SN. TD. TG	E, BF, BJ, CF,
AU S	9184307	•	A1	19930405	AU 1991-84307	19910905 <
	602028 602028		A1 B1		EP 1991-915001	19910905 <
EP (IT, LI, NL, SE	
	06510017		Т2		JP 1991-513470	19910905 <
	3176619 2084176		B2 T3	20010618 19960501	ES 1991-915001	19910905 <
	5663174		A			19970117 <
PRIORITY	APPLN.	INFO.:			EP 1991-915001	A 19910905

Ward 10_663042

WO 1991-EP1678

A 19910905

US 1994-204317

B1 19940304

OTHER SOURCE(S):

MARPAT 119:159909

GI

SO2NH (CH2Ph) CONH (CH2) 6NH2 I

Aromatic sulfonamides ZSO2ANR1R2 [A = direct bond, amino acid residue with AΒ its N atom bound to the SO2 moiety and the carboxyl group bound to the N-atom moiety; R1 = H; R2 = biphenyl, C2-6 alkylene, Ph (only if $Z \neq$ naphthyl or chloronaphthyl and A ≠ direct bond); R1R2 may form a piperazine ring], useful as inhibitors of phospholipase A2 and calcium-dependent enzymes, and which may be of use in the treatment of inflammation, infarct, and arthritis (no data), are prepared Thus, the HCl salt of sulfonamide I, prepared from chloronaphthalenesulfonyl chloride, N-tert-BOC-L-phenylalanine, and N-BOC-6-aminohexane, exhibited 50% inhibition concentration of bovine pancreatic phospholipase A2 at 67 μm.

IT 149569-25-5P 149569-31-3P 149569-33-5P

149569-39-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and calcium-dependent enzyme and phospholipase A2 inhibitory activity of)

RN

149569-25-5 HCAPLUS
Piperazine, 1-[[1-(phenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, CN monohydrochloride, (S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCl

149569-31-3 HCAPLUS RN

CNPiperazine, 1-[[1-[(4-fluorophenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]-, monohydrochloride, (S) - (9CI) (CA INDEX NAME)

● HCl

RN 149569-33-5 HCAPLUS
CN Piperazine, 1-[[1-[(5-chloro-1-naphthalenyl)sulfonyl]-2pyrrolidinyl]carbonyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 149569-39-1 HCAPLUS
CN Piperazine, 1-[[1-(5-isoquinolinylsulfonyl)-2-pyrrolidinyl]carbonyl]-,
dihydrochloride, (S)- (9CI) (CA INDEX NAME)

•2 HCl

IT 149586-38-9P 149586-51-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, as intermediates of calcium-dependent enzyme and phosphokinase inhibitors)

RN 149586-38-9 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[1-(phenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 149586-51-6 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[1-[(4-fluorophenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)

L32 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1990:553044 HCAPLUS

DOCUMENT NUMBER:

113:153044

TITLE:

Process for preparing trans-4-phenyl-L-proline derivatives as intermediates for angiotensin-

converting enzyme (ACE) inhibitors

INVENTOR(S):

Kronenthal, David; Kuester, Paula L.; Mueller, Richard

E. R. Squibb and Sons, Inc., USA PATENT ASSIGNEE(S):

SOURCE:

U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 61,511,

abandoned. CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				-	
US 4912231	Α	19900327	US 1988-209165		19880617 <
CA 1333807	A1	19950103	CA 1988-566007		19880505 <
GB 2205832	A1	19881221	GB 1988-13659		19880609 <
GB 2205832	B2	19910717			
FR 2616431	A1	19881216	FR 1988-7841		19880613 <
FR 2616431	B1	19940812			
JP 01016761	A2	19890120	JP 1988-146690		19880614 <
JP 08032677	B4	19960329			
PRIORITY APPLN. INFO.:			US 1987-61511	В2	19870615
OTHER SOURCE(S):	CASRE	ACT 113:1530	44; MARPAT 113:153044		

O'

GI

$$\mathbb{R}^2$$
 \mathbb{R}^2
 \mathbb

AB Title derivs. I (R = N-protecting group; R1 = H, aryl, alkyl; R2 = H, halo; trans/cis ≥ 90:10) are prepared by Friedel-Crafts-type reaction of cis proline derivs. II (X = leaving group) with benzene, a halobenzene, or PhSiMe3 in the presence of a Lewis acid catalyst a 5-80° under an inert atmospheric The mol ratio of II to aromatic compound to catalyst is 1:(5-100):(2-10)[. For example, trans-4-hydroxy-L-proline was subjected to a sequence of N-benzoylation, Me esterification, O-tosylation, saponification,

lactonization, methanolysis, O-mesylation, and saponification to give II (R = Bz,

R1 = H, X = MeSO3). The mesylate was added to excess benzene and AlCl3, followed by stirring for 7 h at room temperature, cooling, hydrolysis, and workup (2 crops) to give 81% I (R = Bz, R1 = R2 = H). Prepns. of a variety of I and II are described.

IT 120807-08-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as intermediate for ACE inhibitors, via Friedel-Crafts reaction)

RN 120807-08-1 HCAPLUS

CN L-Proline, 1-[(4-methylphenyl)sulfonyl]-4-phenyl-, trans- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L32 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:515737 HCAPLUS

DOCUMENT NUMBER: 111:11573

TITLE: Preparation of trans-4-phenyl-L-proline derivatives as

intermediates for ACE (angiotensin-converting

enzyme) inhibitors

INVENTOR(S): Kronethal, David R.; Kuester, Paula L.; Mueller,

Richard H.

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: Ger. Offen., 17 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

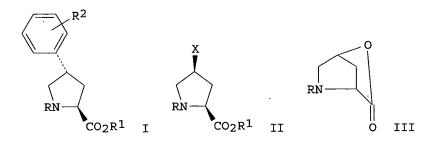
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3820230	A1	19881229	DE 1988-3820230	19880614 <
DE 3820230	C2	20021107		

Ward 10 663042

CA 1333807	A1	19950103	CA 1988-566007		19880505 <
GB 2205832	A1	19881221	GB 1988-13659		19880609 <
GB 2205832	B2	19910717			
FR 2616431	A1	19881216	FR 1988-7841		19880613 <
FR 2616431	B1	19940812			
JP 01016761	A2	19890120	JP 1988-146690		19880614 <
JP 08032677	B4	19960329			
PRIORITY APPLN. INFO.:			US 1987-61511	Α	19870615
OTHER SOURCE(S):	MARPAT	111:115737			
GI					



The title compds. (I; R = protecting group; R1 = H, aryl, alkyl; R2 = H, halo), useful as intermediates for ACE inhibitors, were prepared by aromatic nucleophilic substitution of proline derivative II (X = leaving group) or proline lactone III in the presence of Lewis acid catalysts.

1-Benzoyl-allo-hydroxy-L-proline lactone (preparation from trans-4-hydroxy-L-proline given) and AlCl3 were stirred 2 h at 45° in C6H6 and the mixture was kept for 5 h at room temperature to give 40% I (R = Bz, R1 = R2 = H).

IT 120807-08-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as intermediate for ACE inhibitor)

RN 120807-08-1 HCAPLUS

CN L-Proline, 1-[(4-methylphenyl)sulfonyl]-4-phenyl-, trans- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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STR

Ak Cy Ak O Ak G1 Hy SO2 Cy @10 11 @12 13 14 16 15 8 9

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GRAPH ATTRIBUTES: RSPEC I

NUMBER OF NODES IS

STEREO ATTRIBUTES: NONE L10 STR

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GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10 L13

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 38

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L18
           183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE
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L19
           2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?
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L25
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                "PISSARNITSKI DMITRI A"/AU) NOT (L16 OR L22 OR L32)
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=> d ibib abs 133 1-13
L33 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                         2005:331941 HCAPLUS
TITLE:
                         Optimization of purine based PDE1/PDE5 inhibitors to a
                         potent and selective PDE5 inhibitor for the treatment
                         of male ED
AUTHOR (S):
                         Boyle, Craig D.; Xu, Ruo; Asberom, Theodros;
                         Chackalamannil, Samuel; Clader, John W.; Greenlee,
                         William J.; Guzik, Henry; Hu, Yuequing; Hu, Zhiyong;
                         Lankin, Claire M.; Pissarnitski, Dmitri A.;
                         Stamford, Andrew W.; Wang, Yuguang; Skell, Jeffrey;
                         Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda,
                         Jairam; Chintala, Madhu; Wu, Ping; Myers, Joyce; Wang,
                         Peng
CORPORATE SOURCE:
                         Schering-Plough Research Institute, Kenilworth, NJ,
                         07033, USA
SOURCE:
                         Bioorganic & Medicinal Chemistry Letters (2005),
                         15(9), 2365-2369
                         CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER:
                        Elsevier B.V.
DOCUMENT TYPE:
                        Journal
LANGUAGE:
                        English
     In search of a PDE5 inhibitor for erectile dysfunction, an SAR was
     developed from a PDE1/PDE5 purine series of leads, which had modest PDE5
     potency and poor isoenzyme selectivity. A compound (41) with PDE5
     inhibition and in vivo activity similar to sildenafil was discovered from
     this effort. In addition, purine 41 demonstrated superior overall PDE
     isoenzyme selectivity when compared to the approved PDE5 inhibitors
     sildenafil, vardenafil, and tadalafil, which may result in a more
```

L33 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2004:226370 HCAPLUS

favorable side-effect profile.

TITLE: Discovery of a PDE5 inhibitor for the treatment of

male ED

AUTHOR(S): Boyle, Craig D.; Chackalamannil, Samuel; Lankin, Claire M.; Wang, Yuguang; Hu, Zhiyong; Asberom,

Theodros; Clader, John W.; Greenlee, William J.;

Guzik, Henry; Pissarnitski, Dmitri;

Stamford, Andrew W.; Xu, Ruo; Skell, Jeffrey;

Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Mahdu; Wu, Ping; Myers, Joyce; Wang,

Peng

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 227th ACS National Meeting,

Anaheim, CA, United States, March 28-April 1, 2004

(2004), MEDI-012. American Chemical Society:

Washington, D. C. CODEN: 69FGKM

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Using a stepwise approach to improve upon the phys. and pharmacol. properties of a xanthine lead structure, we discovered a PDE5 inhibitor for the treatment of male ED. This compound improves upon the PDE isoenzyme selectivity, enzyme inhibition, and PK profile of the leading drug on the market, sildenafil (Viagra). This paper will summarize the medicinal

chemical effort toward the discovery of potent and selective PDE5 inhibitors.

L33 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:153600 HCAPLUS

DOCUMENT NUMBER: 140:350038

TITLE: SAR development of polycyclic guanine derivatives

targeted to the discovery of a selective PDE5 inhibitor for treatment of erectile dysfunction

AUTHOR(S): Pissarnitski, Dmitri A.; Asberom, Theodros;

Boyle, Craig D.; Chackalamannil, Samuel; Chintala, Madhu; Clader, John W.; Greenlee, William J.; Hu, Yueqing; Kurowski, Stanley; Myers, Joyce; Palamanda, Jairam; Stamford, Andrew W.; Vemulapalli, Subbarao;

Wang, Yuguang; Wang, Peng; Wu, Ping; Xu, Ruo

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004),

14(5), 1291-1294

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

AB Development of structure-activity relationship of cyclic guanines I lead us to discovery of a potent and selective series of phosphodiesterase 5

inhibitors 52-59 (IC50=1.3-11.0 nM, PDE6/5=116-600).

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:634975 HCAPLUS

TITLE: Discovery of Sch 444877, a potent, selective and

orally active cyclic guanine PDE5 inhibitor

AUTHOR(S): Wang, Yuguang; Chackalamannil, Samuel; Stamford,

Andrew; Boyle, Craig D.; Hu, Zhiyong; Lankin, Claire;

Clader, John; Xu, Ruo; Asberom, Theodros; Pissarnitski, Dmitri; Greenlee, William;

Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda,

Jairam; Chintala, Mahdu; Wu, Ping; Myers, Joyce; Wang,

Peng

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 226th ACS National Meeting, New

York, NY, United States, September 7-11, 2003 (2003), MEDI-367. American Chemical Society: Washington, D.

C.

CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Sch 444877 is a tricyclic guanine derived potent inhibitor of human PDE5 isoenzyme with an IC50 value of 1.5 nM. Its PDE6/PDE5 selectivity is about 250-fold. In the dog pelvic nerve stimulation model, Sch 444877 dose-dependently increased cavernosal pressure with an ED100 slightly more potent than sildenafil. It also showed a rapid onset and fast clearance PK profile.

L33 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:396889 HCAPLUS

DOCUMENT NUMBER: 138:401744

TITLE: Preparation of polycyclic guanine derivative

phosphodiesterase V inhibitors

INVENTOR(S): Asberom, Theodros; Clader, John W.; Hu, Yueqing;

Pissarnitski, Dmitri A.; Stamford, Andrew W.;

Xu, Ruo

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIN	D DATE	APPLICATION NO.	DATE			
WO 2003042216	A1	20030522	WO 2002-US35721	20021107			
W: AE, AG	AL, AM,	AT, AU, AZ,	BA, BB, BG, BR, BY,	BZ, CA, CH, CN,			
CO, CR	CZ, DE,	DK, DM, DZ,	EC, EE, ES, FI, GB,	GD, GE, HR, HU,			
ID, IL	IN, IS,	JP, KG, KR,	KZ, LC, LK, LR, LT,	LU, LV, MA, MD,			
MG, MK	MN, MX,	MZ, NO, NZ,	PH, PL, PT, RO, RU,	SC, SE, SG, SI,			
SK, SL	TJ, TM,	TN, TR, TT,	TZ, UA, UZ, VC, VN,	YU, ZA, ZM			
RW: GH, GM	KE, LS,	MW, MZ, SD,	SL, SZ, TZ, UG, ZM,	ZW, AM, AZ, BY,			
•			BE, BG, CH, CY, CZ,				
FI, FR	GB, GR,	IE, IT, LU,	MC, NL, PT, SE, SK,	TR, BF, BJ, CF,			
•			ML, MR, NE, SN, TD,				
			US 2002-290011				
			EP 2002-786685				
R: AT, BE	CH, DE,	DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,			
•	•		CY, AL, TR, BG, CZ,				
JP 2005509038	T2	20050407	JP 2003-544052	20021107			
PRIORITY APPLN. INFO			US 2001-344498P				
			WO 2002-US35721	W 20021107			
OTHER SOURCE(S):	MAR	PAT 138:4017	14				

^{*} STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

```
AB
     Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl,
     cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y =
     alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-
     (ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate
     (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe,
     reflux, 4 h), subsequently treated with POCl3 and the product used to
     alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which
    provides II. II is treated with MsCl (Et3N), debenzylated (MeOH, NH4O2CH,
     Pd(OH)2/C, reflux, 3 h), brominated (HOAc, NaOAc, Br2), alkylated with
     3-chloro-4-methoxybenzyl bromide (DMF, K2CO3) and treated with NaOEt
     (DMF/EtOH) to afford III. III has IC50 < 4.1 nM for PDE V and IC50 > 300
     nM for PDE VI. I are useful for treating sexual dysfunction.
REFERENCE COUNT:
                         5
                               THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L33 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                         2003:202642 HCAPLUS
DOCUMENT NUMBER:
                         138:238193
TITLE:
                         Preparation of polycyclic guanines for therapeutic use
                         as phosphodiesterase V inhibitors
                         Asberom, Theodros; Hu, Yueqing; Pissarnitski,
INVENTOR(S):
                         Dmitri A.; Xu, Ruo; Wang, Yuguang;
                         Chackalamannil, Samuel; Clader, John W.; Stamford,
                         Andrew W.
PATENT ASSIGNEE(S):
                         Schering Corporation, USA
                         PCT Int. Appl., 179 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
    PATENT NO.
                         KIND
                                           APPLICATION NO.
                                                                   DATE
                                DATE
     _____
                                _____
                                            _____
                         ____
                                          WO 2002-US27181
    WO 2003020724
                         A1
                               20030313
                                                                    20020826
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,
             ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK,
             SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
     CA 2457944
                          AΑ
                                20030313
                                            CA 2002-2457944
                                                                    20020826
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OTHER SOURCE(S): MARPAT 138:238193

Α1

Α1

T2

20030814

20040526

20050127

US 2003153587

JP 2005502684

PRIORITY APPLN. INFO.:

EP 1421084

GΙ

AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2002-227778

JP 2003-524994

US 2001-315395P

WO 2002-US27181

EP 2002-761506

20020826

20020826

20020826

P 20010828

W 20020826

AΒ Purine cyclic derivs., such as I and II [R1 = H, alkyl, cycloalkyl; R2 = N3, CN, oximino, halo, haloalkyl, cycloalkenyl, heteroaryl, etc.; R3 = H, alkyl, arylalkyl, etc.; X = bond, connecting group, such as O, S, SO, SO2, amino, etc.; X1 = (CH2)2, CHR3, etc.; Y = H, alkyl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase V (PDE5) inhibitors. These polycyclic guanines are useful for treatment of physiol. disorders, wherein the physiol. disorder, symptom or disease is urogenital, such as male erectile dysfunction, peripheral vascular, angina pectoris, restenosis post angioplasty, endarterectomy, stent introduction, cerebral stroke, respiratory tract, allergic associated with atopy, pulmonary hypertension, ischemic heart, impaired glucose tolerance, diabetes, neuropathy, insulin resistance syndrome, hyperglycemia, polycystic ovarian syndrome, glomerular renal insufficiency, nephritis, tubular interstitial, autoimmune, glaucoma, intestinal motility, cachexia, cancer, cognitive impairment or nutcracker esophageal. Thus, polycyclic guanine III was prepared via a multistep synthetic sequence which included cyclization of (R)-2-amino-3-phenyl-1-propanol with 2-chloro-1-ethyl-1,7-dihydro-7-(phenylmethyl)-6H-purin-6-one to form the desired cyclic guanine ring, followed sequentially by removal of the benzyl group using Pd(OH)2/C in MeOH, 8-bromination using Br2 and NaOAc, 7-benzylation with 3-chloro-4-methoxybenzyl bromide using K2CO3 in DMF, and finally, alkynylation with phenylacetylene using (PPh3)2PdCl2, CuI and Et3N. The prepared polycyclic guanines were assayed for inhibition of PDE5 activity. REFERENCE COUNT: THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133232 HCAPLUS

DOCUMENT NUMBER: 138:187649

TITLE: Preparation of 1-sulfonyl quinoline derivatives as

γ-secretase inhibitors.

INVENTOR(S): Asberom, Theodros; Guzik, Henry S.; Josien, Hubert B.;

Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P.	ATENT	NO.			KIN	D	DATE			APPL	ICAT	ION I	NO.		D.	ATE	
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WC	2003						2003	0220		WO 2	002-	JS24	323		2	0020	801
	2003														_	0020	
		ΑE,							RΔ	BB	BG.	BB	BV	B7.	CD	CH	CN
							DM,										
							KG,					-		-			-
							NO,						•	•	•		
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EF	1492															0020	
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							RO,										
JI	2005	5047	60		T2		2005	0217		JP 2	003-	5190:	25		2	0020	301
PRIORIT	Y APP	LN.	INFO	. :					1	US 2	001-	3100	13P]	P 2	0010	303
									1	US 2	002-	3555	10P]	P 2	0020	206
									1	WO 2	002-1	JS24:	323	1	W 2	0020	301
סקעקט ס	OTTOCE	101.			MADI	ידי ער	120.	1076	10								

OTHER SOURCE(S): MARPAT 138:187649

GI

$$(R^{4})_{p}$$
 $(R^{3})_{2}$
 $(R^{3})_{2}$
 $(R^{3})_{2}$
 $(R^{3})_{2}$
 $(R^{3})_{2}$
 $(R^{3})_{2}$
 $(R^{3})_{2}$

II

AB Title compds. I [R1 = aryl, heteroaryl; R2 = alkyl, XCOY, etc; R3-3a = H, alkyl; R4 = halo, CF3, OH, alkoxy, etc.; X = O, NH, N-alkyl; Y = amino; m, n = 0-3 such that m + n = 1-4; p = 0-4] are prepared For instance, quinaldic acid is converted to the 2-hydroxymethyl-1,2,3,4-tetrahydroquinoline (MeOH, H2-PtO; MeOH, SOCl2; THF, LAH); this is protected as the TMS-ether derivative and sulfonylated (CH2Cl2, Et3N, TMSCl; Et3N, 4-ClC6H4SO2Cl). This intermediate is desilylated (MeOH, K2CO3), converted to the 4-nitrophenylcarbonate and treated with 1-(3-aminopropyl)imidazole to give II. Selected compds. of the invention have IC50 in the range of about 0.030 to 24.45 μM for γ-secretase. I are useful for the treatment of Alzheimer's Disease.

L33 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133040 HCAPLUS

DOCUMENT NUMBER: 138:170082

mini n

TITLE: Preparation of piperidinylsulfonamides as

 γ -secretase inhibitors

INVENTOR(S): Josien, Hubert B.; Clader, John W.; Asberom, Theodros;

Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE			
WO 2003013527		WO 2002-US24293	20020801			
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY, I	BZ, CA, CH, CN,			
CO, CR, CZ,	DE, DK, DM, DZ,	EC, EE, ES, FI, GB, G	GD, GE, HR, HU,			
ID, IL, IN,	IS, JP, KG, KR,	KZ, LC, LK, LR, LT, 1	LU, LV, MA, MD,			
MG, MK, MN,	MX, MZ, NO, NZ,	PH, PL, PT, RO, RU, S	SE, SG, SI, SK,			
SL, TJ, TM,	TN, TR, TT, TZ,	UA, UZ, VN, YU, ZA,	ZM, AM, AZ, BY,			
KG, KZ, MD,	RU, TJ, TM					
RW: GH, GM, KE,	LS, MW, MZ, SD,	SL, SZ, TZ, UG, ZM, Z	ZW, AT, BE, BG,			
CH, CY, CZ,	DE, DK; EE, ES,	FI, FR, GB, GR, IE,	IT, LU, MC, NL,			
PT, SE, SK,	TR, BF, BJ, CF,	CG, CI, CM, GA, GN, C	GQ, GW, ML, MR,			
NE, SN, TD,	TG					
CA 2455861	AA 20030220	CA 2002-2455861	20020801			
US 2003216380	A1 20031120	US 2002-210803	20020801			
EP 1411944	A1 20040428	EP 2002-761207	20020801			
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IT, LI, LU, 1	NL, SE, MC, PT,			
IE, SI, LT,	LV, FI, RO, MK,	CY, AL, TR, BG, CZ, I	EE, SK			
JP 2005504042	T2 20050210	JP 2003-518536	20020801			
PRIORITY APPLN. INFO.:		US 2001-310068P	P 20010803			
		WO 2002-US24293	W 20020801			
OTHER SOURCE(S):	MARPAT 138:17008	32				

$$(R^1)_{qq}Ar^1SO_2$$
 $(R^2)_{qq}C1$
 $(R^4)_{m}$
 $(R^4)_{p}$
 $(R^4)_{m}$
 $(R^4)_{p}$
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 $(R^4)_{p}$
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 $(R^4)_{p}$
 $(R^4$

AB Title compds. [I; Ar1, Ar2 = aryl, heteroaryl; Y = bond, [C(R3)2]1-3; R1 = halo, CF3, OCF3, cyano, amino, alkyl, alkylaminocarbonyl, (substituted) aryl, heteroaryl, etc.; R2 = alkyl, halo, CF3, OCF3, cyano, NO2, amino, OH, alkoxycarbonyl, alkylaminocarbonyl, alkoxy, aryloxy, etc.; R3 = H, alkyl; R4 = alkyl, OH, alkoxy; R5 = H, alkyl, aryl, heteroaryl, alkoxyalkylene, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, alkylsulfonyl, alkylaminosulfonyl, etc.; m, n, p, q, qq = 0-3], were prepared Thus, 3-amino-1-tert-butoxycarbonylpiperidine, Me 4-formylbenzoate, and 4Å mol. sieves were stirred together in MeOH overnight; NaBH4 was added followed by 3 h stirring to give 85% benzylpiperidinylamine derivative This was stirred 2 days with 4-ClC6H4SO2Cl and Et3N in CH2Cl2 to give 77% title compound (II). I inhibited γ-secretase with IC50 = 0.028-69.550 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:767305 HCAPLUS

DOCUMENT NUMBER: 138:331192

TITLE: Design and synthesis of xanthine analogues as potent

and selective PDE5 inhibitors

AUTHOR(S): Wang, Yuguang; Chackalamannil, Samuel; Hu, Zhiyong;

Boyle, Craig D.; Lankin, Claire M.; Xia, Yan; Xu, Ruo;

Asberom, Theodros; Pissarnitski, Dmitri;

Stamford, Andrew W.; Greenlee, William J.; Skell, Jeffrey; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Madhu; Wu, Ping; Myers,

Joyce; Wang, Peng

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002),

12(21), 3149-3152

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

AB We have discovered potent and selective xanthine PDE5 inhibitors. One compound (PDE5 IC50=0.6 nM, PDE6/PDE5=101) demonstrated similar functional efficacy and pharmacokinetic profile to sildenafil (PDE5 IC50=3.5 nM,

PDE6/PDE5=7).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:815366 HCAPLUS

DOCUMENT NUMBER: 132:222730

TITLE: Stereocontrolled Elaboration of Natural

(-)-Polycavernoside A, a Powerfully Toxic Metabolite

of the Red Alga Polycavernosa tsudai

AUTHOR(S): Paquette, Leo A.; Barriault, Louis; Pissarnitski,

Dmitri; Johnston, Jeffrey N.

CORPORATE SOURCE: Evans Chemical Laboratories, The Ohio State

University, Columbus, OH, 43210, USA

SOURCE: Journal of the American Chemical Society (2000),

122(4), 619-631

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: A
DOCUMENT TYPE: J

American Chemical Society Journal

DOCUMENT TYPE: LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 132:222730

AB A stereoselective total synthesis of natural levorotatory polycavernoside

A has been achieved. Initial investigations produced the properly activated disaccharide unit via the conjoining of building blocks

originating from L-fucose and D-xylose.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1999:283406 HCAPLUS

DOCUMENT NUMBER:

130:338300

TITLE:

An approach to the enantioselective synthesis of polycavernoside a: investigation of sulfur-stabilized carbanion chemistry for union of the southern and

northern fragments of the aglycone

AUTHOR (S):

SOURCE:

Pissarnitski, Dmitri

CORPORATE SOURCE:

Ohio State Univ., Columbus, OH, USA (1998) 235 pp. Avail.: UMI, Order No. DA9911250

From: Diss. Abstr. Int., B 1999, 59(10), 5369

Dissertation

LANGUAGE:

English

AB Unavailable

DOCUMENT TYPE:

L33 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1999:257527 HCAPLUS

DOCUMENT NUMBER:

130:338306

TITLE:

A Convergent Total Synthesis of the Macrolactone

Disaccharide Toxin (-)-Polycavernoside A

AUTHOR(S):

Paquette, Leo A.; Barriault, Louis; Pissarnitski,

Dmitri

CORPORATE SOURCE:

Evans Chemical Laboratories, The Ohio State

University, Columbus, OH, 43210, USA

SOURCE:

Journal of the American Chemical Society (1999),

121(18), 4542-4543

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI

t-BuPh₂SiO

O

O

Me

OH

I

AB Title (-)-polycavernoside A was prepared from lactone I via coupling with disaccharide.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:632427 HCAPLUS

DOCUMENT NUMBER: 129:330944

TITLE: A Modular Enantioselective Approach to Construction of

the Macrolactone Core of Polycavernoside A

AUTHOR(S): Paquette, Leo A.; Pissarnitski, Dmitri;

Barriault, Louis

CORPORATE SOURCE: Evans Chemical Laboratories, The Ohio State

University, Columbus, OH, 43210, USA

SOURCE: Journal of Organic Chemistry (1998), 63(21), 7389-7398

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

GI

AB A program directed toward a total synthesis of polycavernoside A is described. The synthesis of five building blocks is detailed. The first

of two electrophilic units, the lactone (I), was prepared in four steps from the known enantiomerically pure oxirane (II). Pyranyl aldehyde (III) was elaborated in turn from L-malic acid via (IV). While the route to (V) involved I as a starting material, dithiane (VI) was obtained in a straightforward manner from IV as well. The merging of the chiral sectors could not be accomplished by way of the lithiated dithianyl anions, presumably as a consequence of their heightened basicity. The strategic incorporation of the trienyl sector was accomplished, although no attempt was made to control the diastereoselectivity of the process.

REFERENCE COUNT:

THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STR

Ak Cy

 $Ak \sim 0 \sim Ak$

G1~Hy~SO2Cy

@10 11 @12 13 14

16 15 8 9

VAR G1=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/10/12 NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM GGCAT IS MCY AT 15 DEFAULT ECLEVEL IS LIMITED

46

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE L10 STR

VAR G1=1/4/9/14/29 REP G2=(1-5) C NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

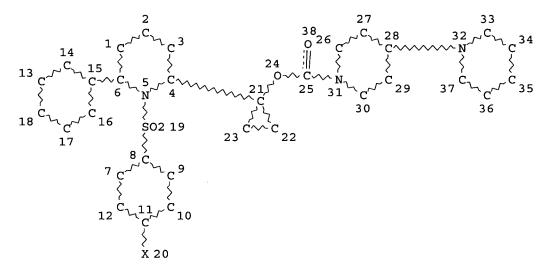
GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10 L13 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

L15	5	SEA FILE=REGISTRY SUB=L12 SSS FUL L13
L16	. 3	SEA FILE=HCAPLUS ABB=ON PLU=ON L15
L17	25432	SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15
L18	183	SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE
L19	3443	SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L20	2011	SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?
L21	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20
L22	6	SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16
L23	450	SEA FILE=HCAPLUS ABB=ON PLU=ON L19(L)INHIBIT?
L24	372	SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND PD= <december 2003<="" 8,="" td=""></december>
L25	301	SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND PATENT/DT
L29	78	SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND ENZYME(L)INHIBIT?
L31	35	SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L25
L32	35	SEA FILE=HCAPLUS ABB=ON PLU=ON L31 NOT (L16 OR L22)
L34	40	SEA FILE=HCAPLUS ABB=ON PLU=ON ("JOSIEN H"/AU OR "JOSIEN H
		B"/AU OR "JOSIEN HUBERT"/AU OR "JOSIEN HUBERT B"/AU) NOT (L16
		OR L22 OR L32)

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=> d ibib abs 1-40

L34 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:15936 HCAPLUS

DOCUMENT NUMBER: 142:114104

TITLE: A preparation of pyrazine derivatives, useful as MCH

antagonists

INVENTOR (S): Palani, Anandan; Shapiro, Sherry A.; Josien,

Hubert B.; Bara, Thomas A.; Clader, John W.;

Pushpavanam, Pradeep B.; Li, Shengjian; Mcbriar, Mark

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 34 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE .

GΙ

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.			KIND DATE		APPLICATION NO.					DATE							
US	US 2005004121			A1	.1 20050106			US 2004-878788						20040628			
WO	WO 2005005419			A1	A1 20050120			WO 2004-US20763					20040628				
	W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BW,	ΒY,	BZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,
		ĻΚ,	LR,	LS,	LT,	LU,	LV,	ΜA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	NI,
		NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
		ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ΖM,	ZW
	RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
		ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
		EE,	ES,	FI,	FR,	GB,	GR,	ΗU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
		SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,
		SN,	TD,	TG													
PRIORITY APPLN. INFO.:							1	US 2	003-4	1836	19P		P 2	0030	530		
OTHER SO	URCE	(S):			MAR	PAT	142:	1141	04								

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention relates to a preparation of pyrazine derivs. of formula I [wherein: Ar is aryl; R1 is C(O) aryl, O-alkyl, halogen, or heteroaryl, etc.; R2 and R3 are independently selected from H, alkyl, or (hetero)aryl; R4 is H or alkyl; R5 is (cyclo)alkyl or aryl], useful as melanin-concentrating hormone (MCH) antagonists (antiobesity agents). For instance, pyrazine derivative II (10nM < Ki < 15nM) was prepared via amidation of 3-propoxythiophene-2-carboxylic acid by pyrazinylpiperidine derivative III with a yield of 54%.

L34 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:239373 HCAPLUS

DOCUMENT NUMBER: 141:1035

TITLE: Chronic Treatment with the γ -Secretase Inhibitor

LY-411575 Inhibits β -Amyloid Peptide Production and Alters Lymphopoiesis and Intestinal Cell

Differentiation

AUTHOR (S): Wong, Gwendolyn T.; Manfra, Denise; Poulet, Frederique

M.; Zhang, Qi; Josien, Hubert; Bara, Thomas;

Engstrom, Laura; Pinzon-Ortiz, Maria; Fine, Jay S.; Lee, Hu-Jung J.; Zhang, Lili; Higgins, Guy A.; Parker,

Eric M.

CORPORATE SOURCE: Chemical Research, Immunology, Departments of Central

Nervous System Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

SOURCE: Journal of Biological Chemistry (2004), 279(13),

12876-12882

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

Biology

DOCUMENT TYPE: Journal LANGUAGE: English

Inhibition of γ -secretase, one of the enzymes responsible for the cleavage of the amyloid precursor protein (APP) to produce the pathogenic β -amyloid (A β) peptides, is an attractive approach to the treatment of Alzheimer disease. In addition to APP, however, several other γ -secretase substrates have been identified (e.g. Notch), and altered processing of these substrates by γ -secretase inhibitors could lead to unintended biol. consequences. To study the in vivo consequences of $\gamma\text{-secretase}$ inhibition, the $\gamma\text{-secretase}$ inhibitor LY-411575 was administered to C57BL/6 and TgCRND8 APP transgenic mice for 15 days. Although most tissues were unaffected, doses of LY-411575 that inhibited Aβ production had marked effects on lymphocyte development and on the intestine. LY-411575 decreased overall thymic cellularity and impaired intrathymic differentiation at the CD4-CD8-CD44+CD25+ precursor stage. No effects on peripheral T cell populations were noted following LY-411575 treatment, but evidence for the altered maturation of peripheral B cells was observed In the intestine, LY-411575 treatment increased goblet cell number and drastically altered tissue morphol. These effects of LY-411575 were not seen in mice that were administered LY-D, a diastereoisomer of LY-411575, which is a very weak γ -secretase inhibitor. These studies show that inhibition of γ -secretase has the expected benefit of reducing A β in a murine model of Alzheimer disease but has potentially undesirable biol. effects

as well, most likely because of the inhibition of Notch processing. REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER:

2003:133232 HCAPLUS

DOCUMENT NUMBER:

138:187649

TITLE:

SOURCE:

Preparation of 1-sulfonyl quinoline derivatives as

 γ -secretase inhibitors

INVENTOR(S):

Asberom, Theodros; Guzik, Henry S.; Josien,

Hubert B.; Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S):

Schering Corporation, USA PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
WO 2003014075	A2	20030220	WO 2002-US24323	20020801		
WO 2003014075	A3	20040930				

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,

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ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD,
             MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK,
             SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    CA 2455863
                                20030220
                                             CA 2002-2455863
                          AΑ
                                                                     20020801
    US 2003135044
                          Α1
                                 20030717
                                             US 2002-210829
                                                                     20020801
    US 6683091
                          B2
                                20040127
    BR 2002011698
                          Α
                                20041109
                                             BR 2002-11698
                                                                     20020801
    EP 1492765
                          A2
                                20050105
                                             EP 2002-759233
                                                                     20020801
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     JP 2005504760
                          T2
                                20050217
                                             JP 2003-519025
                                                                     20020801
                                             US 2001-310013P
PRIORITY APPLN. INFO.:
                                                                    20010803
                                             US 2002-355510P
                                                                    20020206
                                             WO 2002-US24323
                                                                    20020801
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OTHER SOURCE(S): MARPAT 138:187649

$$(R^4)_p$$
 $(R^3)_2$
 $(R^4)_p$
 $(R^3)_2$
 $(R^3)_2$

AB Title compds. I [R1 = aryl, heteroaryl; R2 = alkyl, XCOY, etc; R3-3a = H, alkyl; R4 = halo, CF3, OH, alkoxy, etc.; X = O, NH, N-alkyl; Y = amino; m, n = 0-3 such that m + n = 1-4; p = 0-4] are prepared For instance, quinaldic acid is converted to the 2-hydroxymethyl-1,2,3,4-tetrahydroquinoline (MeOH, H2-PtO; MeOH, SOCl2; THF, LAH); this is protected as the TMS-ether derivative and sulfonylated (CH2Cl2, Et3N, TMSCl; Et3N, 4-ClC6H4SO2Cl). This intermediate is desilylated (MeOH, K2CO3), converted to the 4-nitrophenylcarbonate and treated with 1-(3-aminopropyl)imidazole to give II. Selected compds. of the invention have IC50 in the range of about 0.030 to 24.45 μM for

γ-secretase. I are useful for the treatment of Alzheimer's Disease.

L34 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133040 HCAPLUS

DOCUMENT NUMBER: 138:170082

TITLE: Preparation of piperidinylsulfonamides as

 γ -secretase inhibitors

INVENTOR(S): Josien, Hubert B.; Clader, John W.; Asberom,

Theodros; Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: Facence English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 2003013527	A1 20030220	WO 2002-US24293	20020801
W: AE, AG, AL	AM, AT, AU, AZ,	BA, BB, BG, BR, BY,	BZ, CA, CH, CN,
CO, CR, CZ	DE, DK, DM, DZ,	EC, EE, ES, FI, GB,	GD, GE, HR, HU,
ID, IL, IN	IS, JP, KG, KR,	KZ, LC, LK, LR, LT,	LU, LV, MA, MD,
MG, MK, MN	MX, MZ, NO, NZ,	PH, PL, PT, RO, RU,	SE, SG, SI, SK,
SL, TJ, TM	TN, TR, TT, TZ,	UA, UZ, VN, YU, ZA,	ZM, AM, AZ, BY,
KG, KZ, MD	RU, TJ, TM		
RW: GH, GM, KE	LS, MW, MZ, SD,	SL, SZ, TZ, UG, ZM,	ZW, AT, BE, BG,
CH, CY, CZ	DE, DK, EE, ES,	FI, FR, GB, GR, IE,	IT, LU, MC, NL,
PT, SE, SK	TR, BF, BJ, CF,	CG, CI, CM, GA, GN,	GQ, GW, ML, MR,
NE, SN, TD	TG		
CA 2455861	AA 20030220	CA 2002-2455861	20020801
US 2003216380	A1 20031120	US 2002-210803	20020801
EP 1411944	A1 20040428	EP 2002-761207	20020801
R: AT, BE, CH	DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,
IE, SI, LT	LV, FI, RO, MK,	CY, AL, TR, BG, CZ,	EE, SK
JP 2005504042	T2 20050210	JP 2003-518536	
PRIORITY APPLN. INFO.:		US 2001-310068P	P 20010803
		WO 2002-US24293	W 20020801
OTHER SOURCE(S): GI	MARPAT 138:1700	82	

$$(R^{1})_{qq}Ar^{1}SO_{2} \qquad YAr^{2}(R^{2})_{q} \qquad C1$$

$$n \qquad N$$

$$R^{5} \qquad I \qquad BOC \qquad II$$

AB Title compds. [I; Ar1, Ar2 = aryl, heteroaryl; Y = bond, [C(R3)2]1-3; R1 = halo, CF3, OCF3, cyano, amino, alkyl, alkylaminocarbonyl, (substituted) aryl, heteroaryl, etc.; R2 = alkyl, halo, CF3, OCF3, cyano, NO2, amino, OH, alkoxycarbonyl, alkylaminocarbonyl, alkoxy, aryloxy, etc.; R3 = H, alkyl; R4 = alkyl, OH, alkoxy; R5 = H, alkyl, aryl, heteroaryl,

alkoxyalkylene, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, alkylsulfonyl, alkylaminosulfonyl, etc.; m, n, p, q, qq = 0-3], were prepared Thus, 3-amino-1-tert-butoxycarbonylpiperidine, Me 4-formylbenzoate, and 4\nol mol. sieves were stirred together in MeOH overnight; NaBH4 was added followed by 3 h stirring to give 85% benzylpiperidinylamine derivative This was stirred 2 days with 4-ClC6H4SO2Cl and Et3N in CH2Cl2 to give 77% title compound (II). I inhibited γ -secretase with IC50 = 0.028-69.550 μ M.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:76254 HCAPLUS

DOCUMENT NUMBER: 139:46165

TITLE: Recent advances in the development of

γ-secretase inhibitors

AUTHOR(S): Josien, Hubert

CORPORATE SOURCE: CV and CNS Medicinal Chemistry Department,

Schering-Plough Research Institute, Kenilworth, NJ,

07033-1300, USA

SOURCE: Current Opinion in Drug Discovery & Development

(2002), 5(4), 513-525

CODEN: CODDFF; ISSN: 1367-6733

PUBLISHER: PharmaPress Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Alzheimer's disease is a neurodegenerative disorder that exerts a huge psychol. and social toll in modern societies. The current hypothesis for the cause of this illness is that it is the result of aberrant production of β -amyloid (A β) and plaque deposition in the brain of affected individuals. New therapeutic interventions seek to stop or even reverse the course of the disease by inhibiting this aggregation or reducing A β formation. The use of inhibitors of γ -secretase, a key enzyme in the production of A β , is currently undergoing preclin. and clin. evaluation. Small mol. inhibitors which demonstrate efficacy in reducing A β burden in mice have thus been recently discovered. This review summarizes the development of such inhibitors in light of the current understanding of the function of γ -secretase. It also provides an evaluation of the therapeutic potential for this class of compds. with the recent discovery of other biochem. pathways associated with γ -secretase, such as Notch signaling.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:754356 HCAPLUS

DOCUMENT NUMBER: 137:279095

TITLE: Preparation of N-[biaryl(piperidinyl)ethyl]-N'-

arylureas and analogs as melanin-concentrating hormone

receptor antagonists

INVENTOR(S): Clader, John W.; Josien, Hubert B.; Palani,

Anandan; Chan, Tin-Yau Schering Corporation, USA PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT ASSIGNEE(S):

SOURCE:

Ward 10 663042-inventor search

PATENT NO.			KIND DATE			j	APPL	ICAT	ION	DATE						
WO 2002	WO 2002076947			Δ1 20021003			WO 2002-1109229					20020320				
	AE, AG,															
	CO, CR,			-				-			•			•		
	ID, IL,															
	MG, MK,	MN, I	MX, N	IZ, NO	, NZ,	PH,	ΡL,	PT,	RO,	RU,	SE,	SG,	SI,	SK,		
	SL, TJ,		-	•		UA,	UZ,	VN,	ΥU,	ZA,	ZM,	AM,	ΑZ,	BY,		
	KG, KZ,	•	•	•												
RW:	GH, GM,												-			
	CY, DE,	-		-			-						•	,		
### DODG	BF, BJ,															
	105094															
	239															
	528															
R:	AT, BE,	•		•					ъΙ,	ьU,	ΝL,	SE,	MC,	ΡΤ,		
DD 2002	IE, SI,	•		•					0150			_				
	008150				40302								0020			
	532835 004169				41028								0020			
PRIORITY APP			А	200	21110			003-4 001-2					00309 00101			
PRIORITI APP	IN. INFO.	•						001 002-1					0010.			
OTHER SOURCE	(S) :	1	MARPA	AT 137	:2790			002-0	J303.		,	v 2	0020.	520		

AB Title compds., e.g., RZCH(Z1R1)CH2Z2CONHR2 (Z = piperidine-1,4-diyl, Z1 = 1,4-phenylene)[I; R = H, (cyclo)alkyl, alkylsulfonyl, etc.; R1 = (un)substituted Ph or 3-pyridinyl; R2 = halophenyl, (un)substituted pyridinyl, etc.; Z2 = O or NH] were prepared Thus, BocZCH(Z1Br)CH2OH (preparation given) was aminated and the product condensed with 3,5-Cl2C6H3NCO to give BocZCH(Z2Br)CH2NHCONHC6H3Cl3-3,5 which was converted in 3 steps to title compound II. Data for biol. activity of title compds. were given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

II

L34 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2002:439522 HCAPLUS

DOCUMENT NUMBER:

137:47089

TITLE:

Synthesis, SAR, and Biological Evaluation of Oximino-Piperidino-Piperidine Amides. 1. Orally Bioavailable CCR5 Receptor Antagonists with Potent

Anti-HIV Activity

AUTHOR (S):

Palani, Anandan; Shapiro, Sherry; Josien,

Hubert; Bara, Thomas; Clader, John W.; Greenlee,

William J.; Cox, Kathleen; Strizki, Julie M.; Baroudy,

Bahige M.

CORPORATE SOURCE:

Chemical Research, Schering-Plough Research Institute,

Kenilworth, NJ, 07033, USA

SOURCE:

Journal of Medicinal Chemistry (2002), 45(14),

3143-3160

CODEN: JMCMAR; ISSN: 0022-2623

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

PUBLISHER:

English

OTHER SOURCE(S):

CASREACT 137:47089

GI

AB The discovery of 4-[(Z)-(4-bromophenyl) (ethoxyimino) methyl]-1'-[(2,4dimethyl-3-pyridinyl)carbonyl]-4'-methyl-1,4'-bipiperidine N-oxide (I; SCH 351125), an orally bioavailable human CCR5 antagonist for the treatment of HIV-1 infection, has been reported. The discovery of I from initial lead compds. is discussed as well as synthesis and SAR studies directed toward optimization of substitution at the Ph, oxime, and right-hand side amide groups in the oximino-piperidino-piperidine series. Substitutions (4-Br, 4-F3C, 4-F3CO, 4-MeSO2, and 4-Cl) at the Ph group are well-tolerated, and small alkyl substitutions (Me, Et, Pr, i-Pr, and cyclopropylmethyl) at the oxime moiety are preferred for CCR5 antagonism. The 2,6dimethylnicotinamide N-oxide moiety is the optimal choice for the right-hand side. Several compds. in this series, including I, exhibited excellent antiviral activity in vitro. I, which has a favorable pharmacokinetic profile in rodents and primates, excellent oral bioavailability, and potent antiviral activity against a wide range of primary HIV-1 isolates, is a potentially promising new candidate for treatment of HIV-1 infection.

REFERENCE COUNT:

34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:385004 HCAPLUS

DOCUMENT NUMBER:

136:386137

TITLE:

Preparation of piperidinylpiperazines as CCR5

chemokine receptor antagonists.

INVENTOR(S):

Baroudy, Bahige M.; Clader, John W.; Josien, Hubert B.; McCombie, Stuart W.; McKittrick, Brian A.; Miller, Michael W.; Neustadt, Bernard R.; Palani, Anandan; Smith, Elizabeth M.; Steensma, Ruo; Tagat, Jayaram R.; Vice, Susan F.; Gilbert, Eric; Labroli,

Marc A.

PATENT ASSIGNEE(S):

Schering Corporation, USA

SOURCE:

U.S., 72 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6391865	B1	20020521	US 2000-562814	20000501
US 2003069252	A1	20030410	US 2002-61011	20020130
US 6689765	B2	20040210		
US 2004067961	A1	20040408	US 2003-668862	20030923
PRIORITY APPLN. INFO.:			US 1999-132509P P	19990504
			US 2000-562814 A3	20000501
			US 2002-61011 A3	20020130

OTHER SOURCE(S):

MARPAT 136:386137

GI

Title compds. [I; R = (substituted) Ph, pyridyl, thienyl, naphthyl; R1 = AB H, alkyl; R2 = (substituted) Ph, heteroaryl, naphthyl, fluorenyl, diphenylmethyl, (substituted) phenylalkyl, heteroarylalkyl; R3 = H, alkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, (substituted) Ph, phenylalkyl, naphthyl, naphthylalkyl, heteroaryl, heteroarylalkyl; R4, R5, R7 = H, alkyl; R6 = H, alkyl, alkenyl], were prepared Thus, title compound (II) [preparation starting from (S)-alanine Me ester hydrochloride given] inhibited RANTES binding in a CCR5 membrane binding assay with Ki = 9.97 nM. REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS

HCAPLUS COPYRIGHT 2005 ACS on STN L34 ANSWER 9 OF 40

ACCESSION NUMBER:

2002:367287 HCAPLUS

DOCUMENT NUMBER:

136:369611

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TITLE: Preparation of piperidine derivatives as CCR5

antagonists

INVENTOR(S): Baroudy, Bahige M.; Clader, John W.; Josien,

Hubert B.; McCombie, Stuart W.; McKittrick, Brian
A.; Miller, Michael W.; Neustadt, Bernard R.; Palani,
Anandan; Steensma, Ruo; Tagat, Jayaram R.; Vice, Susan

F.; Laughlin, Mark A.

PATENT ASSIGNEE(S):

Schering Corporation, USA

SOURCE:

U.S., 91 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6387930	B1	20020514	US 2000-562815	20000501
US 2003004185	A1	20030102	US 2001-10481	20011108
US 6602885	B2	20030805	•	
PRIORITY APPLN. INFO.:			US 1999-132510P P	19990504
			US 2000-562815 A3	20000501
OTHER SOURCE(S):	MARPAT	136:369611		

-

Title compds. [I; R = XaRa; Ra = (un) substituted Ph, -pyridyl, -thienyl, -naphthyl; R1 = H or alk(en)yl; R3 = COR2; R2 = halo, alkyl, (un) substituted Ph, ZR7, etc.; R7 = halo, OH, alkyl, OMe, etc.; R14-R16 = H or alkyl; Xa = (un) substituted alkylene, O, CO, NH, etc.; Z = (un) substituted heteroarylene] were prepared Thus, PhBr was acylated by N-trifluoroacetylpiperidine-4-carbonyl chloride and the O-protected-N-deprotected product condensed with N-Boc-4-piperidone in the presence of Ti(OPr)4 followed by treatment with Et2AlCN to give, after MeMgBr treatment, I [R = 4-BrC6H4C(R4)2, R1 = Me, R14-R16 = H](II; R3 = CO2CMe3, R4R4 = OCH2CH2O). The latter was O- and N-deprotected and the product converted in 3 steps to II (R3 = H, R4R4 = NOMe) which was

amidated by 2,6-Me2C6H3CO2H to give title compds. (E) - and (Z)-III. Data for biol. activity of I were given.

REFERENCE COUNT: THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS 19

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:59018 HCAPLUS

DOCUMENT NUMBER: 136:262969

TITLE: Synthesis of Mono- and Difluoronaphthoic Acids AUTHOR (S): Tagat, Jayaram R.; McCombie, Stuart W.; Nazareno, Dennis V.; Boyle, Craig D.; Kozlowski, Joseph A.;

Chackalamannil, Samuel; Josien, Hubert;

Wang, Yuguang; Zhou, Guowei

CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute,

Kenilworth, NJ, 07033-0539, USA

SOURCE: Journal of Organic Chemistry (2002), 67(4), 1171-1177

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:262969

Aryl carboxamides are useful structural units found in several biol. active compds. Unlike their benzoic acid counterparts, fluorinated versions of naphthoic acids are relatively unknown. In connection with a recent project, we needed viable syntheses of several mono- and difluorinated naphthoic acids. Herein we describe the synthesis of 5-, 6-, 7-, and 8-fluoro-1-naphthalenecarboxylic acids and 5,7-, 5,8-, 6,7-, and 4,5-difluoro-1-naphthalenecarboxylic acids. The 5-fluoronaphthoic acid was obtained from the corresponding 5-bromo compound via electrophilic fluorination of the lithio-intermediate. The remaining 6-fluoro-, 7-fluoro-, 8-fluoro-, 5,7-difluoro-, 5,8-difluoro- and 6,7-difluoronaphthoic acids were prepared by a new, general route involving conversion of com. fluorinated phenylacetic acids to 2-(fluoroaryl)glutaric acids with differential ester groups; selective hydrolysis to a mono acid, intramol. Friedel-Crafts cyclization, and aromatization furnished the target structures. An alternative process to assemble a naphthalene skeleton is also presented for the 5,7-difluoroand 5,8-difluoronaphthoic acids. Finally, 4,5-difluoro-1-

naphthalenecarboxylic acid was prepared expeditiously from 1,8-diaminonaphthalene by adapting classical reactions.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:639925 HCAPLUS

TITLE: Synthesis, SAR, and biological evaluation of

4-phenylpiperidine oximes as CCR5 antagonists for the

treatment of HIV-1 infection

Palani, Anandan; Shapiro, Sherry; Clader, John W.; AUTHOR (S):

Greenlee, William J.; Josien, Hubert; Bara,

Tom; Cox, Kathleen; Baroudy, Bahige

CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute,

Kenilworth, NJ, 07033, USA

SOURCE:

Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-106. American Chemical Society: Washington, D.

CODEN: 69BUZP

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The interaction of HIV-1 with the chemokine receptor CCR5 is required for the entry of the virus into macrophages. It is hoped that CCR5 antagonists which block viral entry will represent a new class of anti-HIV-1 agents with potential use in the prevention and treatment of HIV infection. This presentation will outline the synthesis and structure-activity relationship of 4-substituted Ph piperidine oximes, which are potent and selective CCR5 antagonists.

L34 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:639830 HCAPLUS

TITLE:

Pharmacokinetic improvement of benzylidene ketal M2

muscarinic receptor antagonists via aryl amide

modification

AUTHOR (S):

Boyle, Craig D.; Vice, Susan F.; Chackalamannil, Samuel; Clader, John W.; Ford, Jennifer; Greenlee,

William J.; Josien, Hubert B.; McCombie,

Stuart W.; Nazareno, Dennis V.; Tagat, Jayram R.; Wang, Yuguang; Billard, William; Binch, Herbert, III; Crosby, Gordon; Cohen-Williams, Mary; Coffin, Vicki L.; Cox, Kathleen A.; Grotz, Diane E.; Duffy, Ruth A.;

Ruperto, Vilma; Lachowicz, Jean E.

CORPORATE SOURCE:

CV/CNS Chemical Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

SOURCE:

Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001),

MEDI-011. American Chemical Society: Washington, D.

С.

CODEN: 69BUZP

DOCUMENT TYPE:

Conference; Meeting Abstract

LANGUAGE: English

The senile dementia associated with Alzheimer's disease (AD) is correlated with diminished levels of synaptic acetylcholine (ACh) in the brain. Currently available pharmacotherapy for AD addresses this issue using inhibitors of acetylcholinesterase, which is the enzyme responsible for the degradation of ACh. Elevation of synaptic ACh levels could also be achieved by selectively inhibiting presynaptic muscarinic receptors of the M2 subtype, agonist-induced stimulation of which shuts off ACh release. Such an agent must be selective for the M2 receptor, as inhibition of M1 and M3 receptors causes undesired side effects. Previously, we have reported the initial discovery of a novel class of stabilized benzylidene ketal M2 receptor antagonists. We will discuss new targets consisting of aryl amide modifications which not only improved M2 binding and selectivity, but also enhanced the pharmacokinetic properties of the series. These changes led to the discovery of a highly potent and selective M2 antagonist, which demonstrated in vivo efficacy and had good bioavailability in multiple species.

L34 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:628993 HCAPLUS

DOCUMENT NUMBER:

136:47959

TITLE:

Metabolic stabilization of benzylidene ketal M2

muscarinic receptor antagonists via halonaphthoic acid

substitution

AUTHOR (S):

Boyle, C. D.; Chackalamannil, S.; Clader, J. W.; Greenlee, W. J.; Josien, H. B.; Kaminski, J. J.; Kozlowski, J. A.; McCombie, S. W.; Nazareno, D. V.; Tagat, J. R.; Wang, Y.; Zhou, G.; Billard, W.; Binch, H.; Crosby, G.; Cohen-Williams, M.; Coffin, V. L.; Cox, K. A.; Grotz, D. E.; Duffy, R. A.; Ruperto, V.; Lachowicz, J. E.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2001),

11(17), 2311-2314

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

GΙ

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The potential toxicol. liabilities of a previously studied M2 muscarinic antagonist benzylidene ketal were addressed by replacing the methylenedioxyphenyl moiety with a p-methoxyphenyl group, resulting in M2 selective compds. such as (I). Several halogenated naphthamide derivs. of I were studied to improve the pharmacokinetic profile via blockage of oxidative metabolism Compound (II) demonstrated excellent M2 affinity and selectivity, human microsomal stability, and oral bioavailability in rodents and primates.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:201922 HCAPLUS

TITLE: Discovery of potent, orally bioavailable CCR5

antagonists - 2

AUTHOR(S): Palani, A.; Shapiro, S.; Josien, H.; Bara,

T.; Clader, J.; Greenlee, W.; Tagat, J.; Steensma, R.; McCombie, S.; Neustadt, B.; Pushpavanam, P.; Chan, T. M.; Evans, A.; Blythin, D.; Ganguly, A.; Piwinski, J.;

Dan, N.; Baroudy, B.; Endres, M.; Strizki, J.; Vantuno, N.; Cox, Kathleen; Broske, L.; Zhang, X. Chemical Research, Schering-Plough Research Institute,

Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 221st ACS National Meeting, San

Diego, CA, United States, April 1-5, 2001 (2001)

MEDI-027 CODEN: 69FZD4

PUBLISHER: American Chemical Society DOCUMENT TYPE: Journal; Meeting Abstract

LANGUAGE: English

CORPORATE SOURCE:

AB Inhibition of the interaction of HIV-1 with the chemokine receptor CCR5 is required for the entry of the virus into macrophages. It is hoped that CCR5 antagonists which block viral entry will represent a new class of anti-HIV-1 agents with potential use in the prevention and treatment of HIV infection. This presentation will outline the synthesis and structure-activity relationships of a series of piperidine amides, which are potent and selective CCR5 antagonists. Among these is SCH-C, a selective CCR5 antagonist with potent activity in RANTES binding (Ki=2 nM), viral entry (IC50=0.69 nM) and replication assays (IC50=0.06 to 6.5 nM). SCH-C, which shows excellent oral bioavailability (>50%) in rats, dogs and monkeys, is a potential agent for the treatment of HIV infection.

L34 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:201921 HCAPLUS

TITLE: Discovery of potent, orally bioavailable CCR5

antagonists - 1

Tagat, J.; Nazareno, D.; Vice, S.; Lin, S.; Steensma, AUTHOR (S):

R.; Miller, M.; Bauer, A.; McCombie, S.; Palani, A.;

Josien, H.; Clader, J.; Neustadt, B.;

Greenlee, W.; Ganguly, A.; Piwinski, J.; Chan, T. M.; Evans, A.; Dan, N.; Baroudy, B.; Endres, M.; Strizki,

J.; Vantuno, N.; Cox, K.; Broske, L.; Zhang, X.

CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute,

Kenilworth, NJ, 07033, USA

Abstracts of Papers, 221st ACS National Meeting, San SOURCE:

Diego, CA, United States, April 1-5, 2001 (2001)

MEDI-026 CODEN: 69FZD4

American Chemical Society PUBLISHER: Journal; Meeting Abstract DOCUMENT TYPE:

English LANGUAGE:

The interaction of HIV-1 with the transmembrane chemokine receptor CCR5 is known to be a crucial event in the process whereby the virus gains entry to macrophages. It is therefore expected that blockade of this interaction will prevent viral entry, and that mols. which affect this blockade will provide a new class of anti-HIV-1 agents with a mechanism of action distinct from currently used, intracellular protease and reverse-transcriptase inhibitors. Beginning with leads discovered in high-throughput screening, a series of piperidine amides was identified that are potent antagonists of the human CCR5 receptor. The synthesis, structure-activity relationships and antiviral activity of this antagonist series will be described.

L34 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

2001:156283 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 134:326383

Concise formation of 4-benzyl piperidines and related TITLE:

derivatives using a Suzuki protocol

Vice, Susan; Bara, Tom; Bauer, Annette; Evans, C. AUTHOR (S):

Anderson; Ford, Jennifer; Josien, Hubert; McCombie, Stuart; Miller, Michael; Nazareno, Dennis;

Palani, Anandan; Tagat, Jay

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033-0539, USA

Journal of Organic Chemistry (2001), 66(7), 2487-2492 SOURCE:

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal English LANGUAGE:

OTHER SOURCE(S): CASREACT 134:326383

GI

N BOC Ι

An efficient method of constructing 4-benzyl piperidines and related AB substances, e.g. I, is described. Thus, hydroboration of N-Boc-4-methylenepiperidine followed by reaction with PdCl2dppf/Ph3As/DMF/H2/K2CO3 and 2,5-dibromopyridine gave I in 96% yield. This protocol tolerates a wide variation in both reaction partners and

complements the related process of Zhou and Keana.

REFERENCE COUNT: THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS 25

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:70475 HCAPLUS

DOCUMENT NUMBER: 134:266460

TITLE: The cascade radical annulation approach to new

analogues of camptothecins: Combinatorial synthesis of

silatecans and homosilatecans

Curran, Dennis P.; Josien, Hubert; Bom, AUTHOR(S):

David; Gabarda, Ana E.; Du, Wu

Department of Chemistry and Center for Combinatorial CORPORATE SOURCE:

Chemistry, University of Pittsburgh, Pittsburgh, PA,

15260, USA

SOURCE: Annals of the New York Academy of Sciences (2000),

> 922 (Camptothecins), 112-121 CODEN: ANYAA9; ISSN: 0077-8923 New York Academy of Sciences

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

PUBLISHER:

A review with 30 refs. on the cascade radical annulation approach to the camptothecin, combinatorial synthesis of silatecans and homosilatecans. This combinatorial synthetic approach involves two key steps: (1)

N-propargylation of a lactone/pyridone D/E ring fragment and (2) cascade radical annulation of an A-ring isonitrile to form rings B and C. The

synthesis is probably the most flexible and general route to the camptothecin class of mols. The parallel synthesis of several libraries

of silatecan and homosilatecan libraries is summarized. One of the first-generation silatecans, DB-67, is emerging as a serious candidate for cancer chemotherapy.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:819476 HCAPLUS

DOCUMENT NUMBER: 133:362876

TITLE: Methods for preparation of camptothecin analogs having

antitumor activity

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; David,

PATENT ASSIGNEE(S): University of Pittsburgh, USA

U.S., 24 pp., Cont.-in-part of U. S. Ser. No. 436,799. CODEN: USXXAM SOURCE:

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D	ATE	
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US 6150343			Α		2000	1121	1	US 1	997-	9211	02		1	9970	829
US 6211371			B1		2001	0403	1	US 1	998-	7872			1	9980	115
CA 2302226			AA		1999	0304		CA 1	998-	2302	226		1:	9980	826
WO 9909996			A 1		1999	0304	1	WO 1	998-1	US17	683		1:	9980	826
W: AI	, AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
DH	, EE,	ES,	FI,	GB,	GE,	GH,	GM,	HR,	ΗU,	ID,	ΙL,	IS,	JP,	KE,	KG,
KI	, KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
NC	, NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TR,	TT,
U <i>P</i>	, UG,	UZ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM	

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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
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     AU 9892056
                                 19990316
                                             AU 1998-92056
                           A1
                                                                      19980826
     AU 760543
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                                                                      19980826
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                                 20010904
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                                                                      19980826
                                             US 1998-212178
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     US 6455699
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     US 2001029298
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                           A1
                                                                      20010323
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     US 2002193598
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                                                                      20020429
     US 6743917
                           В2
                                 20040601
     US 2003105324
                                 20030605
                                             US 2002-251153
                           A1
                                                                      20020920
     US 2004029835
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                                             US 2003-629432
                           A1
                                                                      20030729
     US 2004063947
                                 20040401
                                             US 2003-663605
                           A1
                                                                      20030916
PRIORITY APPLN. INFO.:
                                             US 1993-85190
                                                                  A2 19930630
                                             US 1995-436799
                                                                  A2 19950508
                                             US 1997-921102
                                                                  Α
                                                                      19970829
                                             US 1998-7872
                                                                  A3 19980115
                                             WO 1998-US17683
                                                                  W
                                                                      19980826
                                             US 1998-212178
                                                                  A1 19981215
                                             US 2000-613968
                                                                  B1 20000711
                                             US 2000-633561
                                                                  A1 20000807
                                             US 2001-815459
                                                                  A3 20010323
                                             US 2002-251153
                                                                  B1 20020920
OTHER SOURCE(S):
                        CASREACT 133:362876; MARPAT 133:362876
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 R^{2} R^{3} R^{4} R^{4} R^{1} R^{2} R^{3} R^{4} R^{4} R^{5} R^{5}

AB Camptothecin derivs. [I; R1 = H, alkyl, alkenyl, alkynyl, alkoxy, aryloxy, carbamoyloxy, halogen, OH, NO2, CN, N3, CHO, hydrazino, -C(O)Rf {Rf = alkyl, haloalkyl, alkoxy, NH2, OH}, NH2, -SRc {Rc = H, -C(O)Rf, alkyl, aryl, -OC(O)Rd or -OC(O)ORd (Rd = alkyl) etc.,}; R2 = OH; R3 = H, F, halogen, NO2, NH2, OH, CN; R4 = H, F, alkyl, alkenyl, alkynyl, alkoxy; R5 = alkyl, propargyl; R6, R7, R8 = alkyl, alkenyl group, alkynyl, aryl or a -(CH2)nR9 group, wherein n is an integer within the range of 1 through 10 and R9 = OH, alkoxy, amino, alkylamino, dialkylamino, halogen, CN, NO2] and their pharmaceutically acceptable salts were prepared as antitumor agents. Thus, [I; R1-R4 = H, R5 = Et, R6-R8 = Me (II)] was prepared via reaction of (III) and Ph isonitrile. II was tested for antitumor activity [IC50 = 3.8 nm vs HL-60 cells; IC50 = 5.6 nm vs. 833K cells; IC50 = 4.2 nm vs DC-3F cells].

REFERENCE COUNT:

GΙ

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:790477 HCAPLUS

DOCUMENT NUMBER:

133:350146

TITLE:

Preparation of piperidine derivatives as CCR5

. antagonists

INVENTOR(S):

Baroudy, Bahige M.; Clader, John W.; Josien, Hubert B.; McCombie, Stuart W.; McKittrick, Brian
A.; Miller, Michael W.; Neustadt, Bernard R.; Palani,

Anandan; Steensma, Ruo; Tagat, Jayaram R.; Vice, Susan

F.; Laughlin, Mark A.

PATENT ASSIGNEE(S):

Schering Corporation, USA PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	PATENT NO.						KIND DATE			APPLICATION NO.									
WO	2000	0665	 59													20000	501		
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		CZ,	DE,	DK,	DM,	DZ	EE,	ES,	FI,	GE	GD	, GE,	HR,	HU,	ID	, IL,	IN,		
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																TR,			
		TZ,	UA,	US,	UΖ,	VN,	YU,	ZA,	AM,	AZ	Z, BY	, KG,	ΚZ,	MD,	RU	TJ,	TM		
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	T2	Z, UG	, ZW,	ΑT,	BE,	CH	CY,	DE,		
		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU	J, MC	, NL,	PT,	SE,	BF	, BJ,	CF,		
		CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE	E, SN	, TD,	TG						
CA	2371	587			AA		2000	1109		CA	2000	-2371	587		:	20000	501		
EP	1175	402			A1		2002	0130		ΕP	2000	-9264	87			20000	501		
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	R, IT	, LI,	LU,	NL,	SE	, MC,	PT,		
		ΙE,	SI,	LT,	LV,	FI,	RO												
BR	2000	0106	07		Α		2002	0213		BR	2000	-1060	7		:	20000	501		
TR	2001						2002	0321		TR	2001	-2001	03213	3	:	20000	501		
	5146						2004	0528		NZ	2000	-5146	75		:	20000	501		
TR	2004	0249	6		T2		2005	0124		TR	2004	-2004	02496	5	:	20000	501		
ZA	2001	0088	67		Α		2003	0127		ZA	2001	-8867			- 2	20011	026		
NO	2001	0053	65		Α		2002	0103		NO	2001	-5365			:	20011	102		
PRIORIT	Y APP	LN.	INFO	. :						US	1999	-3051	87		A2 :	L9990.	504		
										WO	2000	-US11	633		W :	20000	501		
OTHER SO	OURCE	(S):			MARI	PAT	133:	35014	16										

GI

AB Title compds. [I; R = XaRa; Ra = (un) substituted Ph, -pyridyl, -thienyl, -naphthyl; R1 = H or alk(en)yl; R3 = COR2; R2 = halo, alkyl, (un) substituted Ph, ZR7, etc.; R7 = halo, OH, alkyl, OMe, etc.; R14-R16 = H or alkyl; Xa = (un) substituted alkylene, O, CO, NH, etc.; Z = (un) substituted heteroarylene] were prepared Thus, PhBr was acylated by N-trifluoroacetylpiperidine-4-carbonyl chloride and the O-protected-N-deprotected product condensed with N-Boc-4-piperidone in the presence of Ti(OPr)4 followed by treatment with Et2AlCN to give, after MeMgBr treatment, I [R = 4-BrC6H4C(R4)2, R1 = Me, R14-R16 = H](II; R3 = CO2CMe3, R4R4 = OCH2CH2O). The latter was O- and N-deprotected and the product converted in 3 steps to II (R3 = H, R4R4 = NOMe) which was amidated by 2,6-Me2C6H3CO2H to give title compds. (E) - and (Z)-III. Data for biol. activity of I were given.

REFERENCE COUNT:

5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:790476 HCAPLUS

DOCUMENT NUMBER:

133:350248

TITLE:

Preparation of piperazine derivatives useful as CCR5

antagonists

INVENTOR(S):

Baroudy, Bahige M.; Clader, John W.; Josien,

Hubert B.; Mccombie, Stuart W.; Mckittrick, Brian
A.; Miller, Michael W.; Neustadt, Bernard R.; Palani,
Anandan; Smith, Elizabeth M.; Steensma, Ruo; Tagat,

Jayaram R.; Vice, Susan F.; Laughlin, Mark A.;

Gilbert, Eric; Labroli, Marc A.

PATENT ASSIGNEE(S):

Schering Corporation, USA; et al. PCT Int. Appl., 109 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
				
WO 2000066558	A1	20001109	WO 2000-US11632	20000501

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
               W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
        CA 2371583
                                             AA
                                                        20001109
                                                                          CA 2000-2371583
                                                                                                                      20000501
        EP 1175401
                                             A1
                                                        20020130
                                                                             EP 2000-926486
                                                                                                                      20000501
                     AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                       IE, SI, LT, LV, FI, RO
        BR 2000010304
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        TR 200103214
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                                                        20020321
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        ZA 2001008868
                                                        20030127
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        NO 2001005366
                                                        20020103
                                             Α
                                                                             NO 2001-5366
                                                                                                                      20011102
PRIORITY APPLN. INFO.:
                                                                             US 1999-305226
                                                                                                                A2 19990504
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                                                                                                                Α
                                                                                                                     19990504
                                                                             WO 2000-US11632
                                                                                                                W
                                                                                                                     20000501
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OTHER SOURCE(S): MARPAT 133:350248

GΙ

AB The title compds. I [Ra = optionally substituted Ph, pyridyl, thiophenyl, naphthyl; R1 = H, alkyl; R2 = substituted Ph, substituted heteroaryl, naphthyl, fluorenyl, diphenylmethyl or optionally substituted phenyl- or heteroarylalkyl; R3 = H, alkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, or optionally substituted Ph, phenylalkyl, naphthyl, naphthylalkyl, heteroaryl, heteroarylalkyl; R4, R5, R7 = H, alkyl; R6 = H, alkyl, alkenyl], CCR5 antagonists, were prepared E.g., piperazine derivative II was prepared

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:754523 HCAPLUS

DOCUMENT NUMBER: 133:322036

TITLE: Methods for preparation of camptothecin analogs having

antitumor activity

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; Bom,

David; Burke, Thomas G.

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: U.S., 52 pp., Cont.-in-part of U.S. Ser. No. 921,102.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

		PATENT NO.						DATE		APPLICATION NO.									
		6136				A						1998-					- 9981		
												1997-							
		2353										1999-					9991		
		2000									1999-					9991			
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												, SN,			,	,	,	,	
	ΕP	1140	-	-	-	-			-			1999-				1	9991	215	
												, IT,							
						LV,			•	•			•	- •	•			•	
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		7777										2000-							
	NZ	5122	10			Α		2004	1224		NZ	1999-	5122	10		1	9991	215	
	US	2001	0292	98		A 1		2001	1011		US	2001-	8154	59		2	0010	323	
	US	6620	937			B2		2003	0916										
	US	2002	1935	98		A1		2002	1219		US	2002-	1347	81		2	0020	429	
	US	2002 6743	917			B2		2004	0601										
	US	2004	0639	47		A1		2004	0401		US	2003-	6636	05		2	0030	916	
PRIOF	RITY	APP	LN.	INFO	. :						US	1993-	8519	0]	B2 1	9930	630	
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												1998-							
											US	1998-	2121	78	i	A 1	9981	215	
											WO	1998- 1999- 2000-	US29	937	,	W 1	9991	215	
											US	2000-	6139	68]	B1 2	0000	711	
											US	2001-	8154	59	i	A3 2	0010	323	
OTHER	R SC	URCE	(S):			MARI	PAT	133:3	3220	36									

OTHER SOURCE(S):

MARPAT 133:322036

AB Camptothecin derivs. [I; R1,R2 = H, alkyl, alkenyl, benzyl, alkynyl, alkoxy, aryloxy, acyloxy, -OC(O)ORd, {Rd = alkyl, carbamoyloxy, halogen, OH, NO2, CN, N3, CHO, NH2, -SRc (Rc = H, acyl, alkyl, aryl etc.,)}; R3 = H, halogen, NO2, NH2, OH, CN; or R1 + R2 or R2 + R3together form a group of the formula -O(CH2)nO- wherein n represents the integer 1 or 2; R4 = H, a trialkylsilyl group, F, alkyl, alkenyl, alkynyl, alkoxy; R5 = alkyl, allyl, benzyl, propargyl; R6, R7, R8 = alkyl, alkenyl group, alkynyl, aryl

or a -(CH2) nR9 group, wherein n is an integer within the range of 1 through 10 and R9 = OH, alkoxy, amino, alkyl, dialkylamino, halogen, CN, NO2; X = R11, bond; R11 = alkylene, alkenylene] and their pharmaceutically acceptable salts were prepared as antitumor agents. Thus, [I; R1-R4 = H, XSiR6R7R8 = TMS (II)] was prepared via reaction of III and Ph isonitrile. II was tested for antitumor activity [IC50 = 3.8 nm vs HL-60 cells; IC50 = 5.6 nm vs. 833K cells; IC50 = 4.2 nm vs DC-3F cells].

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

2000:421147 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 133:43697

TITLE: Preparation of camptothecin analogs for use as

antitumor agents

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; Bom,

David; Burke, Thomas G. University of Pittsburgh, USA PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 144 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P	PATENT NO.									APPLICATION NO. DATE								
– W		2000										 . 999-1					 9991	 215
"												BR,						
		** .	•	•	•	•	•	•		•	•	GM,		•	•			
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			•	-	-			-				LS,		•	•		•	
					-						-	SD,						
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			RU,	ТJ,	$\mathbf{M}\mathbf{T}$													
		RW:	GH,	GM,	KΕ,	LS,	MW,	SD,	SL,	SZ,	ΤZ,	ŪĠ,	ZW,	ΑT,	BE,	CH,	CY,	DΕ,
			DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
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С	'A	2353	322			AA		2000	0622	(CA 1	999-	2353	822		1	9991	215
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								2002				2000-1					9991	
																	9991.	
	_	5122				А		2004	1224			.999-!						
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												993-		-				
												.995-						
										1	US 1	.997-:	9211	02		A2 1	9970	829
										1	WO 1	.999-1	US29	937	1	W 1	9991:	215
OTHER	THER SOURCE(S):					MAR	РΔТ	133 -	43697	7								

OTHER SOURCE(S): MARPAT 133:43697

GI

$$R^2$$
 R^3
 R^4
 R^6
 R^6

Camptothecin analogs I [R1, R2 = H, OH, NO2, CN, N3, CHO, NH2, NHNH2, SH, AB alkyl, alkenyl, alkynyl, alkoxy, aryloxy, acyloxy, acyl, carbamoyloxy, halogen, acylthio, alkylthio, arylthio, etc.; R3 = H, NO2, NH2, OH, CN, halogen; R2R3 = O(CH2)nO, n = 1, 2; R4 = H, F, alkyl, alkenyl, alkynyl, trialkylsilyl, alkoxy; R5 = allyl, benzyl, propargyl, alkyl; R6 = trialkylsilyl, trialkylsilylalkyl, etc.] were prepared for use as anticancer agents. Thus, I (R1-4 = H, R5 = Et, R6 = SiMe3) was prepared starting from (4S)-4-ethyl-4-hydroxy-6-iodo-1H-pyrano[3,4-c]pyridine-3,8(4H,7H)-dione and (3-bromo-1-propynyl) trimethylsilane. The prepared camptothecin analogs were tested for inhibition of growth of HL-60, 883K, and DC-3F cancer cell lines, for enhancement of topoisomerase I mediated DNA cleavage, and for inhibition of topoisomerase I mediated DNA relaxation.

REFERENCE COUNT: THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:172606 HCAPLUS

DOCUMENT NUMBER: 130:209844

TITLE: Preparation of camptothecin analogs for use as

antitumor agents

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; Bom,

David

Patent

PATENT ASSIGNEE(S): University of Pittsburgh, USA

PCT Int. Appl., 71 pp. SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE:

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 7 PATENT INFORMATION:

PAT	CENT 1	NO.			KIN		DATE			APPL	ICAT	ION 1	NO.		D	ATE		
WO	9909	996					1999	0304	,	WO 1	 998-1	US17	683		1:	9980	826	
											BY,							
		DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM,	HR,	HU,	ID,	ΙL,	IS,	JΡ,	ΚE,	KG,	
		ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	
		NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	ŚG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	
		UA,	UG,	UΖ,	VN,	ΥU,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM		
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,	
		FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	
		CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG							
US	61503	343			Α		2000	1121	ì	US 1	997-	9211	02		19	99708	329	
CA	23022	226			AA		1999	0304	(CA 1:	998-:	2302:	226		19	99808	326	
ΑU	98920	056			A1		1999	0316		AU 1:	998-	9205	5		19	99808	326	
ΑU	76054	43			B2		2003	0515										
ΕP	10173	399			A1		2000	0712]	EP 1:	998-	9445	35		19	9808	326	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	PT,	ΙE,	FI
JР	20015	5135	67		T2		2001	0904	,	JP 2	000-	5073	36		19	9808	326	

PRIORITY APPLN. INFO.: US 1997-921102 A 19970829 US 1993-85190 A2 19930630 US 1995-436799 A2 19950508

WO 1998-US17683 W 19980826

OTHER SOURCE(S): MARPAT 130:209844

GT

AB Camptothecin analogs I [R1, R2 = H, OH, NO2, CN, N3, NH2, CHO, NHNH2, SH, benzyl, alkyl, alkenyl, alkynyl, alkoxyl, aryloxy, acyloxy, carbamoyloxy, halogen, acyl, alkylthio, acylthio, arylthio; R1R2 = -O(CH2)nO-; n = 1, 2; R3 = H, NO2, NH2, OH, CN; R2R3 = -O(CH2)nO-; n = 1, 2; R4 = H, F, alkyl, alkenyl, alkynyl, alkoxyl; R5 = propargyl, alkyl; R6, R7, R8 = alkyl, alkenyl, alkynyl, aryl, -(CH2)mR9; m = 1-10; R9 = OH, NH2, CN, NO2, alkoxy, alkylamino, dialkylamino, halogen] were prepared for use as antitumor agents. Thus, (20S)-7-(trimethylsilyl)camptothecin was prepared in 85% yield by cyclization of (4S)-4-ethyl-4-hydroxy-6-iodo-1H-pyrano[3,4-c]pyridine-3,8(4H,7H)-dione with Me3SiC.tplbond.CCH2Br in DME and DMF at O°. The prepared compds. were tested for enhancement and inhibition of topoisomerase I activity and for inhibition of cancer cell growth of HL-60, 833K, and DC-3F cell lines.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:646607 HCAPLUS

DOCUMENT NUMBER: 130:66743

TITLE: Design of constrained analogs of amino acids and their

incorporation in the sequence of substance P

AUTHOR(S): Ayoub, Mimoun; Brunissen, Alie; Josien, Hubert

; Loffet, Albert; Chassaing, Gerard; Lavielle, Solange Laboratoire de Chimie Organique Biologique, CNRS URA

493, Universite P. et M. Curie, Paris, 75005, Fr.

SOURCE: Actualites de Chimie Therapeutique (1996), 22, 83-92

CODEN: ACHTD9; ISSN: 0338-8999 ·

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

CORPORATE SOURCE:

AB A review with 15 refs. describing strategies developed by the authors for the preparation of non-proteinogenic amino acids, i.e. rotomeric probes of phenylalanine and $C\alpha$ -methylated amino acids, are described. These amino acids have been incorporated into a substance P analog in order to probe the space fillings of the S7 and S8 binding subsites of the neurokinin-1 receptor and the importance of a reinforcement of α -helical structures on activity.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1998:112193 HCAPLUS

DOCUMENT NUMBER:

128:180426

TITLE:

Preparation of piperazine and piperidine derivatives

as muscarinic antagonists

INVENTOR(S):

Lowe, Derek B.; Chang, Wei K.; Kozlowski, Joseph A.; Berger, Joel G.; McQuade, Robert; Barnett, Allen; Sherlock, Margaret; Tom, Wing; Dugar, Sundeep; Chen, Lian-yong; Clader, John W.; Chackalamannil, Samuel; Wang, Yuguang; McCombie, Stuart W.; Tagat, Jayaram R.; Vice, Susan F.; Vaccaro, Wayne D.; Green, Michael J.; Browne, Margaret E.; Asberom, Theodros; Boyle, Craig

D.; Josien, Hubert B.

PATENT ASSIGNEE(S):

Schering Corp., USA PCT Int. Appl., 156 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.			KIND DATE				APP	LICAT	ION :	NO.		Ι	ATE				
		9805	292			A2 19980212			WO 1997-US13383									
	WO	98.05											-					
		W :	ΑL,	AM,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY	CA,	CN,	CZ,	EE,	GE,	HU,	ΙL,
			IS,	JP,	KG,	KR,	KZ,	LC,	LK,	LR,	LT,	LV,	MD,	MG,	MK,	MN,	MX,	NO,
	•		ΝZ,	PL,	RO,	RU,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	UA,	UZ,	VN,	ΥU,
			AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM							
		RW:	GH,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ZW,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,
			GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PΤ,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,
			GN,	ML,	MR,	ΝE,	SN,	TD,	TG									
	US	5889	006			Α		1999	0330		US 3	L996-	7006	28		1	9960	808
		2261	_			AΑ		1998	0212		CA :	L997-	2261	725		3	9970	806
-	ΑU	9738	999	•		A1		1998	0225		AU :	L997-	3899	9		1	9970	806
	ΑU	7240	01			B2		2000	0907									
		9384				A2		1999	0901		EP :	L997-	9362	96	•	1	9970	806
	ΕP	9384	83			В1		2003	0226									
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	PT,	ΙE,
			LT,	LV,	FI,	RO									•			
	BR	9711	119			Α		1999	1123			1997-						
	JP	2000	5011	17		T2	•	2000	0202		JP :	998-	5080	38		1	9970	806
	NZ	3338	01			Α		2000			NZ :	997-	3338	01		1	9970	806
	AT	2332	60			E		2003	0315		AT :	L997-	9362	96		1	9970	806
	NO	9900	551			Α		1999				1999-						
	HK	1018	776			A1		2003	0829		HK 1	.999-	1037	89		1	9990	902
PRIOR	RIT!	APP	LN.								US 1	1996-	7006	28		A 1	9960	808
											US 1	1995-	3926	97]	B2 1	9950	223
											US 1	L995-	4577	12]	B2 1	9950	602
											US 1	1996-	6024	03		A2 1	9960	216
											WO 1	997-1	US13	383	1	W 1	9970	806

OTHER SOURCE(S):

MARPAT 128:180426

GI

AB Title compds. I (R = OH, HOCH2, etc.; R1 = H, alkyl, alkenyl, cyano, etc.; R2 = H, (un) substituted piperidine; R3 = cycloalkylalkyl, haloacyl, benzyloxalkyl, etc.; R4 = H, halo, alkyl, alkoxy, etc.; R5 = H, alkyl, alkenyl, cyano, etc.; R1-R5 = (un) substituted saturated (hetero) cyclic ring; R6 = H, alkyl, hydroxyalkyl, arylalkyl, aminoalkyl, etc.; R7 = indolylalkyl, carboxyalkyl, etc.; X = O, S, SO, SO2,CO, CS, NHCOO, etc.; RX = I, Br, alkylcarbonyl, etc.; Y = N, CH, C-alkyl; Z = N, CH, C-alkyl), including isomers, salts, esters, and solvates, are prepared and are defined muscarinic antagonists useful for treating cognitive disorders such as Alzheimer's disease. Pharmaceutical compns. and methods of preparation are also disclosed. Also disclosed are synergistic combinations of I with acetylcholinesterase inhibitors.

L34 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:63390 HCAPLUS

DOCUMENT NUMBER: 128:154267

TITLE: A general synthetic approach to the (20S)-camptothecin

family of antitumor agents by a regiocontrolled cascade radical cyclization of aryl isonitriles

AUTHOR(S): Josien, Hubert; Ko, Sung-Bo; Bom, David;

Curran, Dennis P.

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh,

Pittsburgh, PA, 15260, USA

SOURCE: Chemistry--A European Journal (1998), 4(1), 67-83

CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:154267

A general and efficient synthesis of (20S)-camptothecin (I) was reported. A key common intermediate containing the pyridone and lactone (DE) rings of camptothecin and most derivs. was constructed from 2-trimethylsilyl-6methoxypyridine by a series of metalation reactions and a Heck cyclization to provide an achiral bicyclic enol ether. Sharpless asym. dihydroxylation followed by lactol oxidation and iododesilylation produced the key intermediate in 94% enantiomeric excess. Alkylation with propargyl bromide and a cascade radical reaction with PhNC then produced I. About 20 other penta- and hexacyclic analogs of camptothecin with differing single or multiple substituents at C7, C9, C10, C11, and/or C12 were made by changing the propargylating agent and the isonitrile. Included among these are several drug candidates and the approved drugs topotecan and irinotecan. The synthesis of the prodrug irinotecan is a direct one that does not pass through the active metabolite. ortho-trimethylsilyl-substituted isonitriles allows the regioselective synthesis of camptothecin analogs in cases where isomeric mixts. are formed from the parent isonitriles. The synthesis of the derivs. relies

on the broad scope and functional group tolerance of the key cascade radical reaction.

REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L34 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:30511 HCAPLUS

DOCUMENT NUMBER: 128:175876

TITLE: 7-Silylcamptothecins (silatecans): a new family of

camptothecin antitumor agents

AUTHOR(S): Josien, Hubert; Bom, David; Curran, Dennis

P.; Zheng, Yu-Huang; Chou, Ting-Chao

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh,

Pittsburgh, PA, 15260, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997),

7(24), 3189-3194

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compound, 11-fluoro-10-amino-7-

trimethylsilylcamptothecin, is more than 20 times more potent than

camptothecin in cell assays.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:439256 HCAPLUS

DOCUMENT NUMBER: 127:95436

TITLE: Synthesis of (S)-mappicine and mappicine ketone via

radical cascade reaction of isonitriles

AUTHOR(S): Josien, Hubert; Curran, Dennis P.

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh,

Pittsburgh, PA, 15260, USA

SOURCE: Tetrahedron (1997), 53(26), 8881-8886

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 127:95436

GI

AB (S)-mappicine (I) and mappicine ketone were prepared from Me acetoacetate by a strategy featuring a radical cascade reaction of II with Ph isonitrile

as the key step. The introduction of the hydroxy group of (S)-mappicine occurred with moderate selectivity through asym. hydroxylation.

REFERENCE COUNT: THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS 20

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

1997:108748 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 126:207591

TITLE: Tachykinin NK-1 receptor probed with constrained

analogs of substance P

Sagan, Sandrine; Josien, Hubert; Karoyan, AUTHOR (S):

Philippe; Brunissen, Alie; Chassaing, Gerard;

Lavielle, Solange

CORPORATE SOURCE: Laboratoire de Chimie Organique Biologique, CNRS URA

493, Universite P. et M. Curie, Paris, 75005, Fr.

SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(12),

2167-2178

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier DOCUMENT TYPE: Journal LANGUAGE: English

The action of rotameric probes introduced either in position 7 or 8 in the

sequence of substance P (SP) was investigated. i.e., Ltetrahydroisoquinoleic acid (Tic), L-fluorenylglycine (Flg),

L-diphenylalanine (Dip), the diastereoisomers of L-1-indanylqlycine (Inq)

and L-benz[f]indanylglycine (Bfi), the Z- and E-isomers of dehydrophenylalanine and dehydronaphthylalanine (Δ ZPhe, Δ EPhe, $\Delta ZNal$, $\Delta ENal$) and L-o,o'-dimethylphenylalanine (Dmp). The aim this study was the topog. characterization of the binding subsites of human NK-1 receptor expressed in CHO cells, especially the S7 and S8 subsites, corresponding to residues Phe7 and Phe8 of substance P. According to the

binding potencies of these substituted-SP analogs, the S7 binding subsite is smaller than the S8 subsite: the S7 subsite accepts only one aromatic nucleus, while the S8 can accommodate three coplanar nuclei altogether. These findings are compatible with the idea that the S8 binding subsite may reside in the extracellular loops of the hNK-1 receptor. NK-1 agonists bind to human NK-1 receptor and activate the production of both inositol phosphates and cAMP. As already quoted for septide, [pGlu6, Pro9]SP(6-11), discrepancies are observed between affinity (Ki) and activity (EC50) values for IPs production While a weak correlation between Ki and EC50 values for IPs production could be found (r=0.70), an excellent correlation could be demonstrated between their affinities (Ki) and their potencies

(EC50) for cAMP production (r=0.97). The high potency (EC50) observed for "septide-like" mols. on PI hydrolysis, compared to their affinity is not an artifact related to the high level of NK-1 receptors expressed on CHO cells since a good correlation was found between EC50 values obtained for PI hydrolysis and those measured for spasmogenic activity in quinea pig ileum bioassay (r= 0.94).

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

1996:535176 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 125:276262

TITLE: Tandem radical reactions of isonitriles with

> 2-pyridonyl and other aryl radicals: scope and limitations, and a first generation synthesis of

(±)-camptothecin

AUTHOR (S): Curran, Dennis P.; Liu, Hui; Josien, Hubert;

Ko, Sung-Bo

CORPORATE SOURCE: Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260,

USA

SOURCE: Tetrahedron (1996), 52(35), 11385-11404

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 125:276262

GI

I Et CO2Me II

AB Photolysis of N-propargyl-6-halo-2-pyridones and related aromatic halides in the presence of aryl isonitriles provides tetra- and penta-cyclic products, e.g. I and II, in a single step by a sequence of radical addition to the isonitrile followed by two cyclizations. The scope and limitations of the process are described along with a first generation synthesis of racemic camptothecin.

L34 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:463810 HCAPLUS

DOCUMENT NUMBER: 125:133045

TITLE: Topographic analysis of the S7 binding subsite of the

tachykinin neurokinin-1 receptor

AUTHOR(S): Josien, Hubert; Convert, Odile; Berlose,

Jean-Philippe; Sagan, Sandrine; Brunissen, Alie;

Lavielle, Solange; Chassaing, Gerard

CORPORATE SOURCE: Lab. Chim., Univ. Pierre et Marie Curie, Paris, 75005,

Fr.

SOURCE: Biopolymers (1996), 39(2), 133-147

CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Conformationally and configurationally restricted rotameric probes of phenylalanine have been incorporated in the sequence of substance P (SP)-Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH2-for analyzing the binding pockets of Phe7 (S7) and Phe8 (S8), in the neurokinin-1 receptor. These analogs of phenylalanine are (2S, 3R)- and (2S, 3S)-indanylglycines, E- and Z-α, β-dehydrophenylalanines, and 2(S)-α, β-cyclopropylphenylalanines [ΔΕΡhe, ΔΖΡhe, ΔΕ2(S) Phe, and ΔΖ2(S) Phe]. Binding data obtained with either conformationally (Ing diastereoisomers) or configurationally (ΔΕΡhe, ΔΖPhe) probes have unveiled large differences in the binding potencies of these rotameric probes. With the support of NMR data and energy calcns. done on these SP-substituted analogs, we attempt to answer questions inherent to such study. First, none of these six probes

prevents the formation of bioactive conformation (s) of the backbone of SP. Second, both diastereoisomers (S, S) and (S, R) of indanylglycine preferentially adopt, in the sequence of SP, the gauche(-) and trans side-chain orientations, resp., as previously postulated from energy calcns. with model peptides. However, in solution, the difference in energy between these rotamers included in the sequence of SP, compared to model peptides, is smaller since the other rotamer can be detected in [(2S, 3R)Ing7]SP. Finally, from this study we can hypothesize that the large variations observed in the affinities of Phe7 substituted analogs of SP must come from steric hindrance in the S7 binding site, which drastically restricts the space filling around the $C\alpha$ - $C\beta$ bond of residue 7.

L34 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:366335 HCAPLUS

DOCUMENT NUMBER: 125:55785

TITLE: Use of conformationally constrained peptides for a

topographical analysis of the combining site of a

monoclonal anti-substance P antibody

AUTHOR(S): Dery, O.; Josien, H.; Grassi, J.; Chassaing,

G.; Couraud, J. Y.; Lavielle, S.

CORPORATE SOURCE: Serv. Pharmacologie Immunologie, CEA, Gif-sur-Yvette,

91191, Fr.

SOURCE: Biopolymers (1996), 39(1), 67-74

CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AΒ The topog. of the binding site of a monoclonal anti-substance P antibody directed toward the C-terminal pentapeptide of substance P, Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH2, was analyzed further using a wide range of constrained analogs of substance P. Results obtained in the present study show the following: (a) The binding subsites of Phe7 and Phe8 are large and deep, accommodating various side chains, including nonarom. amino acids. (B) In contrast, the binding pockets for Gly-Leu-Met-NH2 appear more restrictive. Consequently, five residues in the peptide are necessary for the high binding affinity to the antibody, the C-terminal tripeptide determining the binding specificity. These data, which appear to contradict those previously published, illustrate the limits of conclusions drawn from studies generally carried out using exclusively Ala-substituted peptides. In addition, the present results indicate that the topog, of the binding site of this monoclonal antibody differs from that of the specific substance P neurokinin-1 receptor, in agreement with the differences observed in the fine specificities of these two substance P binding macromols.

L34 ANSWER 33 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:48103 HCAPLUS

DOCUMENT NUMBER: 124:176598

TITLE: Cascade radical reactions of isonitriles: a

second-generation synthesis of (20S)-camptothecin,

topotecan, irinotecan, and GI-147211C

AUTHOR(S): Curran, Dennis P.; Ko, Sung-Bo; Josien, Hubert

CORPORATE SOURCE: Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260,

USA

SOURCE: Angewandte Chemie, International Edition in English

(1996), Volume Date 1995, 34(23/24), 2683-4

CODEN: ACIEAY; ISSN: 0570-0833

PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S):

CASREACT 124:176598

GI

AB A highly convergent second-generation synthesis of the title compds was achieved from 2-bromo-6-methoxypyridine via the lactone I, which was combined with propargyl bromides and aryl isonitriles in as few as two steps.

L34 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1995:978013 · HCAPLUS

DOCUMENT NUMBER:

124:145849

TITLE:

Selective N-functionalization of 6-substituted-2-

pyridones

AUTHOR(S):

Liu, Hui; Ko, Sung-Bo; Josien, Hubert;

Curran, Dennis P.

CORPORATE SOURCE:

Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260,

USA

SOURCE:

Tetrahedron Letters (1995), 36(49), 8917-20

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER:

Elsevier Journal

DOCUMENT TYPE:

Doulliai

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 124:145849

AB 6-Substituted-2-pyridones can be selectively N-alkylated by treatment with NaH/LiBr in a mixture of DMF and DME. Yields of N-propargylated,

N-allylated, and other N-functionalized products are good, and only small

amts. of the isomeric O-alkylated product (<10%) are typically formed.

The sodium hydride/lithium bromide-mediated propargylation of

6-bromo-2-pyridone with propargyl bromide gave 141807503 (84% yield).

L34 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1994:316363 HCAPLUS

DOCUMENT NUMBER:

120:316363

TITLE:

AUTHOR (S):

Design and Synthesis of Side-Chain Conformationally

Restricted Phenylalanines and Their Use for

Structure-Activity Studies on Tachykinin NK-1 Receptor

Josien, Hubert; Lavielle, Solange;

Brunissen, Alie; Saffroy, Monique; Torrens, Yvette; Beaujouan, Jean-Claude; Glowinski, Jacques; Chassaing,

Gerard

CORPORATE SOURCE:

Laboratoire de Chimie Organique Biologique, Universite

P. et M. Curie, Paris, 75005, Fr.

SOURCE:

Journal of Medicinal Chemistry (1994), 37(11),

1586-601

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Constrained analogs of phenylalanine have been conceptually designed for

analyzing the binding pockets of Phe7 (S7) and Phe8 (S8), two aromatic residues important for the pharmacol. properties of substance P (SP), i.e., L-tetrahydroisoquinoline-2-carboxylic acid, L-diphenylalanine, L-9-fluorenylglycine (Flg), 2-indanylglycine, the diastereomers of L-1-indanylglycine (Ing) and L-1-benz[f]indanylglycine (Bfi), and the Z and E isomers of dehydrophenylalanine (AZPhe, AEPhe). Binding studies were performed with appropriate ligands and tissue prepns. allowing the discrimination of the three tachykinin binding sites, neurokinin-1 (NK-1), NK-2, and NK-3. The potencies of these agonists were evaluated in the guinea pig ileum bioassay. According to the binding data, it is concluded that the S7 subsite is small, as only the gauche (-) probe [(2S,3S)-Ing7]SP presents a high affinity for specific NK-1 binding sites. Surprisingly, the [AEPhe7]SP analog, which projects the aromatic ring toward the trans orientation, is over 40-fold more potent than the Z isomer, [AZPhe7]SP. A plausible explanation of these conflictual results is that either the binding protein quenches the minor trans rotamer of [(2S,3S)-Ing7]SP in solution or this constrained amino acid side chain rotates when inserted in the protein. In position 8, the high binding affinities of [Flg8]SP and[(2S,3S)-Bfi8]SP suggest that the S8 subsite is large enough to accept two aromatic rings in the gauche (-) and one aromatic ring in the trans direction. Peptides bearing two conformational probes in positions 7, 8, or 9 led to postulate that S7, S8, and S9 subsites are independent from each other. The vols. available for side chains 7 and 8 are estimated as close to 110 and 240 Å3, resp. The large volume of the S8 subsite raises question on the localization of the SP-binding site in the NK-1 receptor. If SP were to bind in the transmembrane domains, the cleft defined by the 7 transmembrane segments must rearrange during the binding process in order to bind a peptide in an α -helical structure and at least one large binding subsite in position 8. Thus, indirect topog. anal. with constrained amino acids might contribute to the anal. of the receptor/ligand dynamics. Finally, this study demonstrates that a good knowledge of the peptide backbone structure and a combination of constrained amino acids are prerequisites to confidently attribute the preferred orientation(s) of an amino acid side chain.

L34 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:102419 HCAPLUS

DOCUMENT NUMBER: 118:102419

TITLE: Asymmetric synthesis of the diastereoisomers of

L-1-indanylglycine and L-1-benz[f]indanylglycine,

 $\chi 1, \chi 2$ -constrained side-chain derivatives of L-phenylalanine and L-2-naphthylalanine

AUTHOR(S): Josien, Hubert; Chassaing, Gerard

CORPORATE SOURCE: Lab. Chim. Org. Biol., Univ. Pierre-et-Marie Curie,

Paris, Fr.

SOURCE: Tetrahedron: Asymmetry (1992), 3(11), 1351-4

CODEN: TASYE3; ISSN: 0957-4166

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 118:102419

GI

AB The diastereoisomers of the title compds., novel topog. tools and analogs of phenylalanine and 2-naphthylalanine, were synthesized from sultam-derived glycine imine synthon I alkylated by judicious electrophiles, and subsequent hydrolysis and sultam-cleavage. An x-ray anal. on one alkylation product established the β -configuration.

L34 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:235112 HCAPLUS

DOCUMENT NUMBER: 116:235112

TITLE: A general synthesis of 1-nitro-2-phenyl-4-

oxospiro[2.5]octanes

AUTHOR(S): Dauzonne, Daniel; Josien, Hubert;

Demerseman, Pierre

CORPORATE SOURCE: Serv. Chim., Inst. Curie, Paris, F-75231, Fr.

SOURCE: Synthesis (1992), (3), 309-14 CODEN: SYNTBF; ISSN: 0039-7881

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 116:235112

GI

The title compds. were prepared by a facile two-step route starting from (2-chloro-2-nitroethyl) benzene and 1-morpholino-1-cyclohexene via the base-induced cyclopropanations of the intermediate 2-(2-chloro-2-nitro-1-phenylethyl) cyclohexanones. Michael addition reaction of 1-morpholino-1-cyclohexene with (2-chloro-2-nitroethenyl) benzene gave only a pair of diastereomeric 2-(2-chloro-2-nitro-1-phenylethyl) cyclohexanones I (R = Cl, Rl = H) and I (R = H, Rl = Cl) in 92% overall yield and in a 62:38 diastereomer ratio, resp. Cyclopropanation of I (R = Cl, Rl = H) and I (R = H, Rl = Cl) gave 1-nitro-2-phenyl-4-oxospiro[2.5] octanes II (R2 = H; R3 = NO2, R4 = Ph, R5 = H) in 53% yield and II (R2 = NO2; R3 = H, R4 = H, R5 = Ph) in 40% yield.

L34 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:84146 HCAPLUS

DOCUMENT NUMBER: 116:84146

TITLE: Asymmetric synthesis of L-diphenylalanine and

L-9-fluorenylglycine via room temperature alkylations

of a sultam-derived glycine imine

Josien, Hubert; Martin, Arnaud; Chassaing, AUTHOR (S):

Gerard

CORPORATE SOURCE: Lab. Chim. Org. Biol., Univ. Pierre et Marie Curie,

Paris, Fr.

SOURCE: Tetrahedron Letters (1991), 32(45), 6547-50

CODEN: TELEAY; ISSN: 0040-4039

CHPh₂

'nн

Ph

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 116:84146

GI

Me Me Me Me $\tilde{\text{SO}}_2$ Ph Ph 3

L-Diphenylalanine and L-9-fluorenylglycine were prepared from a AΒ sultam-derived glycine imine 3 via room temperature-asym.alkylation/hydrolysis/mild-sultam-cleavage. The L-configuration was ascertained using an x-ray anal. of the alkylation product 4b.

L34 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:164057 HCAPLUS

DOCUMENT NUMBER: 114:164057

(2-Chloro-2-nitroethenyl) benzenes as synthons: a TITLE:

general method for the preparation of 2,3-dihydro-2-nitro-3-phenyl-4H-furo[3,2-

c][1]benzopyran-4-ones and 3-phenyl-4H-furo[3,2-

4b

c][1]benzopyran-4-ones

Dauzonne, Daniel; Josien, Hubert; AUTHOR (S):

Demerseman, Pierre

Serv. Chim., Inst. Curie, Paris, F75231, Fr.
Tetrahedron (1990), 46(21), 7359-71 CORPORATE SOURCE:

SOURCE:

CODEN: TETRAB; ISSN: 0040-4020

DOCUMENT TYPE: Journal LANGUAGE: English

CASREACT 114:164057 OTHER SOURCE(S):

GT

NO2
H
R3
R1
R1
CH=CC1NO2
R3
II

$$R^3$$
 R^3
 $R^$

AB A convenient and general method for the preparation of dihydronitrophenylfurobenzopyranones (I; R,R1,R2 = H, C1, NO2, OMe; R3 = H, OMe) from 4-hydroxycoumarin and (chloronitroethenyl)benzenes (II) in the presence of KF is described. By replacing KF in the above reaction with Et3N the hitherto unknown phenylfurobenzopyranones (III) are obtained in a one-pot process.

L34 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:102796 HCAPLUS

DOCUMENT NUMBER: 114:102796

TITLE: Synthesis of conformationally constrained

phenylalanines and their incorporation into

tachykinins

AUTHOR(S): Chassaing, G.; Josien, H.; Lavielle, S.

CORPORATE SOURCE: Lab. Chim. Org. Biol., Univ. Paris VI, Paris, F-75005,

Fr.

SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp.,

11th (1990), Meeting Date 1989, 935-6. Editor(s): Rivier, Jean E.; Marshall, Garland R. ESCOM Sci.

Pub.: Leiden, Neth.

CODEN: 56XTA7

DOCUMENT TYPE: Conference

LANGUAGE: English

AB A symposium report on the synthesis of title phenylalanines, e.g. fluorenylglycine and diphenylalanine, and their incorporation into

tachykinins.

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L4 STR

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VAR G1=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/10/12

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DEFAULT ECLEVEL IS LIMITED

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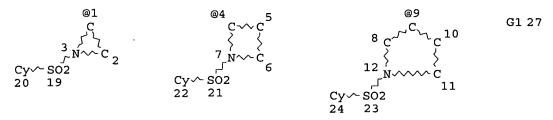
RSPEC I

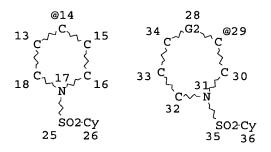
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STEREO ATTRIBUTES: NONE

L10

STR





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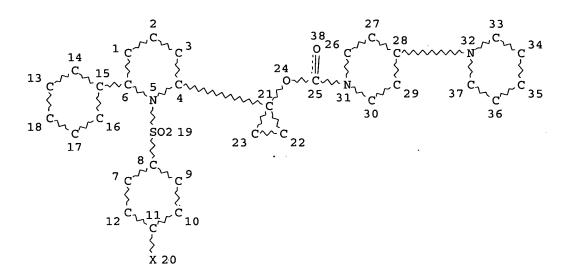
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NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

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L13 STR



NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

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L18	183	SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE
L19	3443	SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L20	. 2011	SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?
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L29	. 78	SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND ENZYME(L)INHIBIT?
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L34	40	SEA FILE=HCAPLUS ABB=ON PLU=ON ("JOSIEN H"/AU OR "JOSIEN H
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L35 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2005:331941 HCAPLUS

TITLE:

Optimization of purine based PDE1/PDE5 inhibitors to a potent and selective PDE5 inhibitor for the treatment

of male ED

AUTHOR(S): Boyle, Craig D.; Xu, Ruo; Asberom, Theodros;

Chackalamannil, Samuel; Clader, John W.; Greenlee, William J.; Guzik, Henry; Hu, Yuequing; Hu, Zhiyong; Lankin, Claire M.; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Wang, Yuguang; Skell, Jeffrey; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Madhu; Wu, Ping; Myers, Joyce; Wang, Peng Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

CORPORATE SOURCE:

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005),

15(9), 2365-2369

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

AB In search of a PDE5 inhibitor for erectile dysfunction, an SAR was developed from a PDE1/PDE5 purine series of leads, which had modest PDE5 potency and poor isoenzyme selectivity. A compound (41) with PDE5 inhibition and in vivo activity similar to sildenafil was discovered from this effort. In addition, purine 41 demonstrated superior overall PDE isoenzyme selectivity when compared to the approved PDE5 inhibitors sildenafil, vardenafil, and tadalafil, which may result in a more favorable side-effect profile.

L35 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:226370 HCAPLUS

TITLE: Discovery of a PDE5 inhibitor for the treatment of

male ED

AUTHOR(S): Boyle, Craig D.; Chackalamannil, Samuel; Lankin,

Claire M.; Wang, Yuguang; Hu, Zhiyong; Asberom,
Theodros; Clader, John W.; Greenlee, William J.;
Guzik, Henry; Pissarnitski, Dmitri; Stamford, Andrew
W.; Xu, Ruo; Skell, Jeffrey; Kurowski, Stanley;
Vemulapalli, Subbarao; Palamanda, Jairam; Chintala,

Mahdu; Wu, Ping; Myers, Joyce; Wang, Peng

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 227th ACS National Meeting,

Anaheim, CA, United States, March 28-April 1, 2004

(2004), MEDI-012. American Chemical Society:

Washington, D. C. CODEN: 69FGKM

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Using a stepwise approach to improve upon the phys. and pharmacol. properties of a xanthine lead structure, we discovered a PDE5 inhibitor for the treatment of male ED. This compound improves upon the PDE isoenzyme selectivity, enzyme inhibition, and PK profile of the leading drug on the market, sildenafil (Viagra). This paper will summarize the medicinal chemical effort toward the discovery of potent and selective PDE5 inhibitors.

L35 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:153600 HCAPLUS

DOCUMENT NUMBER: 140:350038

TITLE: SAR development of polycyclic guanine derivatives

targeted to the discovery of a selective PDE5 inhibitor for treatment of erectile dysfunction

AUTHOR(S): Pissarnitski, Dmitri A.; Asberom, Theodros;

Boyle, Craig D.; Chackalamannil, Samuel; Chintala,

Madhu; Clader, John W.; Greenlee, William J.; Hu, Yueqing; Kurowski, Stanley; Myers, Joyce; Palamanda, Jairam; Stamford, Andrew W.; Vemulapalli, Subbarao;

Wang, Yuguang; Wang, Peng; Wu, Ping; Xu, Ruo

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

Bioorganic & Medicinal Chemistry Letters (2004), SOURCE:

14(5), 1291-1294 CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

Journal DOCUMENT TYPE: English LANGUAGE:

Development of structure-activity relationship of cyclic guanines I lead us to discovery of a potent and selective series of phosphodiesterase 5

inhibitors 52-59 (IC50=1.3-11.0 nM, PDE6/5=116-600).

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 13

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:634975 HCAPLUS

Discovery of Sch 444877, a potent, selective and TITLE:

orally active cyclic guanine PDE5 inhibitor

Wang, Yuguang; Chackalamannil, Samuel; Stamford, AUTHOR (S):

Andrew; Boyle, Craig D.; Hu, Zhiyong; Lankin, Claire;

Clader, John; Xu, Ruo; Asberom, Theodros;

Pissarnitski, Dmitri; Greenlee, William; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Mahdu; Wu, Ping; Myers, Joyce; Wang, Peng

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

Abstracts of Papers, 226th ACS National Meeting, New SOURCE:

York, NY, United States, September 7-11, 2003 (2003), MEDI-367. American Chemical Society: Washington, D.

C.

CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

Sch 444877 is a tricyclic guanine derived potent inhibitor of human PDE5 isoenzyme with an IC50 value of 1.5 nM. Its PDE6/PDE5 selectivity is about 250-fold. In the dog pelvic nerve stimulation model, Sch 444877 dose-dependently increased cavernosal pressure with an ED100 slightly more potent than sildenafil. It also showed a rapid onset and fast clearance PK profile.

L35 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

2003:396889 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 138:401744

Preparation of polycyclic guanine derivative TITLE:

phosphodiesterase V inhibitors

Asberom, Theodros; Clader, John W.; Hu, INVENTOR(S):

Yueqing; Pissarnitski, Dmitri A.; Stamford, Andrew W.;

Xu, Ruo

PATENT ASSIGNEE(S): Schering Corporation, USA

PCT Int. Appl., 95 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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 PRIORITY APPLN. INFO.:
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                                                 WO 2002-US35721 W 20021107
 OTHER SOURCE(S): MARPAT 138:401744
 GT
 * STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
· AB
      Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl,
       cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y =
      alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-
       (ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate
       (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe,
       reflux, 4 h), subsequently treated with POCl3 and the product used to
      alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which provides II. II is treated with MsCl (Et3N), debenzylated (MeOH, NH4O2CH,
      Pd(OH)2/C, reflux, 3 h), brominated (HOAc, NaOAc, Br2), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K2CO3) and treated with NaOEt
       (DMF/EtOH) to afford III. III has IC50 < 4.1 nM for PDE V and IC50 > 300
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L35 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

5

ACCESSION NUMBER: 2003:202642 HCAPLUS

DOCUMENT NUMBER: 138:238193

REFERENCE COUNT:

TITLE: Preparation of polycyclic guanines for therapeutic use

nM for PDE VI. I are useful for treating sexual dysfunction.

as phosphodiesterase V inhibitors

INVENTOR(S): Asberom, Theodros; Hu, Yueqing;

Pissarnitski, Dmitri A.; Xu, Ruo; Wang, Yuguang; Chackalamannil, Samuel; Clader, John W.; Stamford,

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Andrew W.

PATENT ASSIGNEE(S): Schering Corporation, USA SOURCE: PCT Int. Appl., 179 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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     WO 2003020724
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PRIORITY APPLN. INFO.:
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OTHER SOURCE(S):
                         MARPAT 138:238193
GI
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AB Purine cyclic derivs., such as I and II [R1 = H, alkyl, cycloalkyl; R2 = N3, CN, oximino, halo, haloalkyl, cycloalkenyl, heteroaryl, etc.; R3 = H, alkyl, arylalkyl, etc.; X = bond, connecting group, such as O, S, SO, SO2, amino, etc.; X1 = (CH2)2, CHR3, etc.; Y = H, alkyl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase V (PDE5) inhibitors. These polycyclic guanines are useful for treatment of physiol. disorders, wherein the physiol. disorder, symptom or disease is urogenital, such as male erectile dysfunction, peripheral vascular, angina pectoris, restenosis post angioplasty, endarterectomy, stent introduction, cerebral stroke, respiratory tract, allergic associated with atopy, pulmonary

hypertension, ischemic heart, impaired glucose tolerance, diabetes, neuropathy, insulin resistance syndrome, hyperqlycemia, polycystic ovarian syndrome, glomerular renal insufficiency, nephritis, tubular interstitial, autoimmune, glaucoma, intestinal motility, cachexia, cancer, cognitive impairment or nutcracker esophageal. Thus, polycyclic guanine III was prepared via a multistep synthetic sequence which included cyclization of (R)-2-amino-3-phenyl-1-propanol with 2-chloro-1-ethyl-1,7-dihydro-7-(phenylmethyl)-6H-purin-6-one to form the desired cyclic guanine ring, followed sequentially by removal of the benzyl group using Pd(OH)2/C in MeOH, 8-bromination using Br2 and NaOAc, 7-benzylation with 3-chloro-4-methoxybenzyl bromide using K2CO3 in DMF, and finally, alkynylation with phenylacetylene using (PPh3)2PdCl2, CuI and Et3N. prepared polycyclic quanines were assayed for inhibition of PDE5 activity. REFERENCE COUNT: THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:767305 HCAPLUS

DOCUMENT NUMBER: 138:331192

TITLE: Design and synthesis of xanthine analogues as potent

and selective PDE5 inhibitors

AUTHOR(S): Wang, Yuguang; Chackalamannil, Samuel; Hu, Zhiyong;

Boyle, Craig D.; Lankin, Claire M.; Xia, Yan; Xu, Ruo;

Asberom, Theodros; Pissarnitski, Dmitri;

Stamford, Andrew W.; Greenlee, William J.; Skell, Jeffrey; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Madhu; Wu, Ping; Myers,

Joyce; Wang, Peng

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002),

12(21), 3149-3152

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have discovered potent and selective xanthine PDE5 inhibitors. One compound (PDE5 IC50=0.6 nM, PDE6/PDE5=101) demonstrated similar functional efficacy and pharmacokinetic profile to sildenafil (PDE5 IC50=3.5 nM,

PDE6/PDE5=7).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:136921 HCAPLUS

DOCUMENT NUMBER: 137:93725

TITLE: Synthesis and structure-Activity relationships of

M2-Selective muscarinic receptor ligands in the 1-[4-(4-Arylsulfonyl)-phenylmethyl]-4-(4-piperidinyl)-

ria (4 Affationy), phenylmeenyl, 4-(4-pipelidinyl)

piperazine family

AUTHOR(S): McCombie, Stuart W.; Lin, Sue-Ing; Tagat, Jayaram R.;

Nazareno, Dennis; Vice, Susan; Ford, Jennifer; Asberom, Theodros; Leone, Daria; Kozlowski,

Joseph A.; Zhou, Guowei; Ruperto, Vilma B.; Duffy,

Ruth A.; Lachowicz, Jean E.

CORPORATE SOURCE: Department of Chemistry, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002),

12(5), 795-798

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:93725

The synthesis and muscarinic binding properties of compds. based on the 1-[[4-(4-arylsulfonyl)phenyl]methyl]-4-(1-aroyl-4-piperidinyl)piperazine skeleton are described. For compds. substituted with appropriately configured Me groups at the benzylic center and at the piperazine 2-position, high levels of selective, M2 subtype affinity could be obtained, particularly when the terminal N-aroyl residue was ortho substituted.

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 12 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:516896 HCAPLUS

DOCUMENT NUMBER: 135:282588

TITLE: Muscarinic agonists and antagonists in the treatment

of Alzheimer's disease

Greenlee, W.; Clader, J.; Asberom, T.; AUTHOR (S):

McCombie, S.; Ford, J.; Guzik, H.; Kozlowski, J.; Li, S.; Liu, C.; Lowe, D.; Vice, S.; Zhao, H.; Zhou, G.; Billard, W.; Binch, H.; Crosby, R.; Duffy, R.; Lachowicz, J.; Coffin, V.; Watkins, R.; Ruperto, V.;

Strader, C.; Taylor, L.; Cox, K.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033-0539, USA

Farmaco (2001), 56(4), 247-250 CODEN: FRMCE8; ISSN: 0014-827X SOURCE:

Elsevier Science S.A. PUBLISHER: DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review with refs. Alzheimer's disease (AD) is a neurodegenerative disease characterized by cognitive impairment and personality changes. The development of drugs for the treatment of the cognitive deficits of AD has focused on agents which counteract loss in cholinergic activity. Although symptoms of AD have been successfully treated with acetylcholinesterase inhibitors (tacrine, donepezil, rivastigmine, galanthamine), limited success has been achieved with direct M1 agonists, probably due to their lack of selectivity vs. other muscarinic receptor subtypes. Muscarinic M2 antagonists have been reported to increase synaptic levels of acetylcholine after oral administration to rats (e.g. BIBN-99, SCH-57790), but their selectivity vs. other muscarinic receptor subtypes is modest. Exploration of a series of piperidinylpiperidines has yielded the potent and selective M2 antagonist SCH-217443. This antagonist has excellent bioavailability in rats and dogs and shows activity in a rat model of cognition.

REFERENCE COUNT: THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS 12 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:202249 HCAPLUS

TITLE: Discovery of potent, non-peptide thrombin receptor

antagonists

AUTHOR (S): Chackalamannil, Samuel; Xia, Yan; Clasby, Martin;

Greenlee, William; Doller, Dario; Eagen, Keith; Tsai,

Hsingan; Asberom, Theodros; Lin, Yan;

Czarniecki, Michael; Ahn, Ho-Sam; Foster, Carolyn;

Boykow, George

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

Abstracts of Papers, 221st ACS National Meeting, San SOURCE:

Diego, CA, United States, April 1-5, 2001 (2001)

MEDI-342 CODEN: 69FZD4

PUBLISHER: American Chemical Society DOCUMENT TYPE: Journal; Meeting Abstract

LANGUAGE: English

In addition to its key role in hemostasis and wound healing, thrombin activates specific cell surface receptors known as protease-activated receptors (PAR). Activation of thrombin receptor stimulates proliferative and proinflammatory processes in a variety of cell types and may have implications in thrombosis, atherosclerosis, and restenosis. As such, a thrombin receptor antagonist may have considerable utility in the treatment of these diseases. Since a thrombin receptor antagonist is specific for the cellular actions of thrombin and does not interfere with the coagulation cascade, such agents are likely to confer added safety margin with regard to hemorrhagic side effects. Through high throughput screening, we have identified 2-iminobenzimidazole derivs. as well as synthetic analogs of the natural product himbacine as thrombin receptor antagonists. Systematic SAR studies in these classes of compds. led to thrombin receptor antagonists with single digit-nanomolar IC50 values. These compds. inhibited thrombin as well as peptide agonist-induced human platelet aggregation in a dose-dependent manner.

L35 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:202070 HCAPLUS

Discovery of SCH 211803: A potent and highly selective TITLE:

muscarinic M2 antagonist and a promising new approach

to the treatment of alzheimer's disease

AUTHOR (S): Asberom, Theodros; Billard, William; Binch,

Herbert; Clader, John W.; Cox, Kathleen; Crosby, Gordon; Duffy, Ruth A.; Ford, Jenifer; Greenlee, William; Guzik, Henry; Kozlowski, Joseph A.;

Lachowicz, Jean E.; Li, Shengjian; Liu, Charles; Lowe, Derek; McCombie, Stuart; Ruperto, Vilma B.; Strader, Catherine; Taylor, Lisa A.; Vice, Susan; Zhao,

Hongrong; Zhou, Guowei CV/CNS Chemical Research, Schering-Plough Research CORPORATE SOURCE:

Institute, Kenilworth, NJ, 07033, USA

Abstracts of Papers, 221st ACS National Meeting, San SOURCE:

Diego, CA, United States, April 1-5, 2001 (2001)

MEDI-169 CODEN: 69FZD4

PUBLISHER: American Chemical Society DOCUMENT TYPE: Journal; Meeting Abstract

LANGUAGE: English

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by AB a profound cognitive impairment that progresses eventually to an inability to function independently and ultimately to death. One of the consistent findings in the brains of AD patients is loss of cholinergic neurons in the regions of the brain known to be involved in learning and memory. The cholinergic approach to treatment of AD involves counteracting this loss in cholinergic activity by pharmacol. intervention. One approach to improving cholinergic activity is to raise acetylcholine levels through the use cholinesterase inhibitors. These compds. have shown modest efficacy in the clinic due in part to dose-limiting side effects. Another approach to increasing acetylcholine levels is through inhibition of presynaptic muscarinic M2 receptors that control acetylcholine release. This approach has not been successful in the past due to the absence of

compds. that show sufficient selectivity vs. other muscarinic receptors. We now describe the discovery of a class of potent and highly selective muscarinic M2 antagonists typified by SCH 211803. These compds. show=100x selectivity for the M2 receptor vs. other muscarinic receptors and are active in animal models of cognition. They also show a preclin. profile that is indicative of a superior safety profile compared with cholinesterase inhibitors. Thus, this class of compds. represents a promising new approach to the treatment of AD.

L35 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

2000:323253 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 132:334655

TITLE: preparation of himbacine analogs as thrombin receptor

antagonists

Chackalamannil, Samuel; Asberom, Theodros; INVENTOR(S):

Xia, Yan; Doller, Dario; Clasby, Martin C.;

Czarniecki, Michael F.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE:

U.S., 161 pp.

DOCUMENT TYPE:

CODEN: USXXAM

LANGUAGE:

Patent

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				-	
US 6063847	A	20000516	US 1998-197442		19981123
US 6326380	B1	20011204	US 2000-545720		20000407
PRIORITY APPLN. INFO).:		US 1997-66518P	P	19971125
-			US 1998-197442	A3	19981123

OTHER SOURCE(S): MARPAT 132:334655

GI ·

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Heterocyclic-substituted tricyclics of the formula (I) [single dotted line AB represents an optional double bond; double dotted line represents an optional single bond; n = 0-2; Q = (un) substituted cycloalkyl, heterocycloalkyl, aryl or heteroaryl; Het = (un)substituted mono-, bi- or tricyclic heteroarom. group; B = -(CH2)n3-, wherein n3 is 0-5, -CH2-O-, -CH2S-, -CH2-NR6-, -C(O)NR6-. -NR6C(O)-, etc.; X = -O- or -NR6- when the double dotted line represents a single bond, or X is -OH or -NHR20 when the bond is absent; Y = = 0, = S, (H, H), (H, OH) or (H, alkoxy) when the double dotted line represents a single bond, or when the bond is absent, Y =O, (H, H), (H, OH), (H, SH) or (H, C1-C6 alkoxy); R15 is absent when the double dotted line represents a single bond and is H, -NR18R19, or -OR17 when the bond is absent; or Y = -0-(CH2)m-0- or -S-(CH2)m-S-, m = 1-2; and R15, R17, R18, R19 = H or alkyl, aryl etc.] or a pharmaceutically acceptable salt were synthesized. Thus (II) was prepared starting from (R)-3-butyn-2-ol and via condensation of fragment (III) and [5-[3-(trifluoromethyl)phenyl]-2-pyridinyl]methyl-phosphonic acid di-Et ester. II shows an IC50 of 0.11 nM in in vitro thrombin receptor antagonist assay. Phamaceutical compns. containing I as well as method of treating diseases associated with thrombosis, atherosclerosis, restenosis, hypertension, angina pectoris, arrhythmia, heart failure, and cancer are described.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

1999:582651 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 131:214192

TITLE: Preparation of arylaminopiperidines as muscarinic M2

antagonists for treating memory loss

INVENTOR(S): Asberom, Theodros; Lowe, Derek B.; Green,

Michael J.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 28 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5952349	Α	19990914	US 1997-889486	19970708
PRIORITY APPLN. INFO.:			US 1996-21691P P	19960710
OTHER SOURCE(S):	MARPAT	131:214192		

GΙ

AB Title compds. [I; X = bond, O, S, SO, SO2, CO, C(OR7)2, CH2O, CH:CH, CH2, CHA, CA2, CONR17, SO2NR17, etc.; R = cycloalkyl, (substituted) Ph, pyridyl, indolyl, quinolyl, etc.; R1 = H, cyano, CF3, A, cycloalkyl, cycloalkenyl, alkenyl, COR15, CO2A, etc.; R2 = cycloalkyl, cycloalkenyl, BOC, (substituted) 4-piperidinyl; A = alkyl; R3, R4 = H, halo, CF3, A, alkoxy, OH; R5, R6 = H, A, CF3, alkoxy, OH, alkylcarbonyl, alkoxycarbonyl, etc.; R7 = H, A; R15 = H, A, cycloalkyl, aryl, heteroaryl; R17 = H, alkyl, aryl, heteroaryl], were prepared Thus, I (R = 3,4-methylenedioxyphenyl; X = SO2; R1 = cyano; R2 = cyclohexyl; R3-R6 = H) showed Ki = 0.44 nM for binding to M2 receptors.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

1999:355771 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 131:32085

TITLE: Preparation of himbacine analogs for use as thrombin

receptor antagonists

Chackalamannil, Samuel; Asberom, Theodros; INVENTOR(S):

Xia, Yan; Doller, Dario; Clasby, Martin C.;

Czarniecki, Michael F.

PATENT ASSIGNEE(S): Schering Corporation, USA SOURCE:

PCT Int. Appl., 134 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	rent :	NO.			KIN)	DATE		A	APP	LICAT	ION I	NO.			DATE	
											1998 <i>-</i>						
	W:	AL,	AM,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY	, CA,	CN,	CZ,	EE,	. GE), GE,	HR,
											, LK,						
		MN,	MX,	NO,	NZ,	PL,	RO,	RU,	SG,	SI	, SK,	SL,	ТJ,	TM,	TF	TT,	UA,
•											, RU,						•
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SZ,	ŪĠ,	ZW	, AT,	BE,	CH,	CY,	DE	, DK,	ES,
											, PT,						
											, TG					. ,	•
CA	2309	352			AA		1999	0603	С	:A :	1998-	2309	352			19981	.123
CA	2309	352			C		2005	0125									
AU	9914	158			A1		1999	0615	A	U.	1999-	1415	8			19981	.123
	7472																
ZA	9810	685			Α		1999	1223	Z	A :	1998-	1068	5			19981	.123
EP	1036	072			A1		2000	0920	E	P :	1998-	9580	39			19981	.123
EP	1036				BI		2004	0506									
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE	, PT,	ΙE,
	2000										2000-						
BR	9812	793			Α						1998-					19981	123
JP	2001 3449	5244	79		T2		2001		J	IP :	2000-	5221	01			19981	.123
JP	3449	620			B2		2003										
JP	2003	1286	70		A2		2003		J	IP 2	2002-	3150	15			19981	
RU	2204	557			C2				R	?U 2	2000-	1165	48				
TT	135/	9 /			ΑŢ						1998-						
	2660										1998-						
	1036	072			T						1998-						
	2219				Т3				E	is :	1998-	9580	39				
NO	2000	0026	59		Α		2000	0724	N	10 :	2000-	2659				20000	524
	1031				A1		2004	0930	Н	IK :	2001- 2001- 1997-	1018	99			20010	316
PRIORITY	Y APP	LN.	INFO	.:					U	IS :	1997-	9779	79	1	A.	19971	125
											2000-						
											1998-1	US24!	523	7	N	19981	123
OTHER SO	OURCE	(S):			MARI	PAT	131:	32085	5								

OTHER SOURCE(S):

MARPAT 131:32085

Page 59

II

Himbacine analogs I [R = heteroaryl, such as pyridinyl, quinolinyl, AB isoquinolinyl, etc; R1, R2, R8, R10, R11 = H, alkyl, fluoroalkyl, cycloalkyl, alkenyl, aryl, heteroaryl, etc.; R3 = H, OH, alkoxy, alkylsulfinyl, alkylsulfonyl, alkyl, carboxyl, carbamido, aryl, etc.; R4, R5 = H, OH, alkyloxy, alkyl, amino, etc.; R4R5 = O, S; R6 = H; R6R10 = bond; R7R12 = fused alicyclic, fused aryl, fused heteroaryl, etc.; R9 = H, OH, alkoxy, halogen, haloalkyl; X = O, NR13; R13 = H, alkyl, Ph, etc.; Y = (CH2)n, n = 0 - 2; Z = connecting group, such as CH:CH, CH2CH2, CH2O,CH2S, CH2NH, CONH, etc.] were prepared for use as thrombin receptor antagonists for the treatment of diseases associated with thrombosis, atherosclerosis, restenosis, hypertension, angina pectoris, arrhythmia, heart failure, and cancer. Thus, lactone II was prepared starting from (R)-3-butyn-2-ol, trans-3-(1-cyclohexenyl)acrylic acid, and 6-hydroxyquinaldine via the formation and intramol. cycloaddn. of diester III. The prepared compds. were tested for thrombin receptor binding, platelet aggregation and antitumor activity.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

1999:212795 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 130:267454

Preparation of muscarinic antagonists TITLE:

Lowe, Derek B.; Chang, Wei K.; Kozlowski, Joseph A.; INVENTOR(S):

Berger, Joel G.; Mcquade, Robert; Barnett, Allen; Sherlock, Margaret; Tom, Wing; Dugar, Sundeep; Chen, Lian-yong; Clader, John W.; Chackalamannil, Samuel; Wang, Yuguang; McCombie, Stuart W.; Tagat, Jayaram R.; Vice, Susan F.; Vaccaro, Wayne; Green, Michael J.;

Browne, Margaret E.; Asberom, Theodros;

Boyle, Craig D.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 602,403.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT :	NO.			KIN		DATE			APPL	ICAT	ION 1	NO.		Di	ATE	
US	5889	006					1999	0330	•	 US 1	.996-	7006	 28		1	 9960	 808
US	5883	096			Α		1999	0316			996-					9960:	
zA	9601	293			Α		1996	0819		ZA 1	996-	1293			1:	9960	219
zA	9707	011			Α		1998	0206		ZA 1	997-	7011			1:	9970	806
CA	2261	725			AA		1998	0212	1	CA 1	997-	2261	725		1:	9970	806
WO	9805	292			A2		1998	0212	. 1	WO 1	997-1	US13:	383		1:	9970	806
WO	9805	292			A3		1998	0402									
	W:	AL,	AM,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CN,	CZ,	EE,	GE,	HU,	IL,
		IS,	JP,	KG,	KR,	KZ,	LC,	LK,	LR,	LT,	LV,	MD,	MG,	MK,	MN,	MX,	NO,
		ΝZ,	PL,	RO,	RU,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	UA,	UZ,	VN,	YU,
		AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM							
	RW:	GH,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	ΒE,	CH,	DE,	DK,	ES,	FI,	FR,
		GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,
		GN,	ML,	MR,	ΝE,	SN,	TD,	TG									
ΑU	9738	999			A1		1998	0225		AU 1	.997-:	3899	9		1	9970	806
AU	7240	01			B2		2000	0907									
EΡ	9384	83			A2		1999	0901		EP 1	997-	9362	96		1:	9970	806

EP	93848	33			В1		2003	0226											
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	?, I	Τ,	LI,	LU,	NL,	SE	, P	Τ,	ΙE,
		LT,	LV,	FI,	RO														
CN	12324	162			Α		1999	1020		CN	199	7 - :	1984	79			199	708	306
CN	1084	743			В		2002	0515											
BR	9711	119			Α		1999	1123		BR	199	7 - :	1111	9			199	708	306
JP	20009	50111	L7		T2		2000	0202		JP	199	8 - 9	5080	38			199	708	306
NZ	33380	01			Α		2000	0428		NZ	199	7-:	3338	01			199	708	306
AT	23326	50			E		2003	0315		ΑT	199	7 - 9	9362	96			199	708	306
ES	21933	391			Т3	٠	2003	1101		ES	199	7 - 9	9362	96			199	708	306
NO	99009	551			Α		1999	0407		NO	199	9-!	551				199	902	05
KR	20000	02994	17		Α		2000	0525		KR	199	9-'	7011	75			199	902	808
US	60432	255			Α		2000	0328		US	199	9-2	2660	79			199	903	10
HK	10187	776			A1		2003	0829		НK	199	9-:	1037	89			199	909	02
PRIORITY	APPI	LN.]	NFO	. :						US	199	5 - 3	3926	97		В2	199	502	23
										US	199	5 - 4	1577	12		В2	199	506	02
										US	199	6-6	5024	03		A2	199	602	16
										US	199	6-1	7006	28		Α	199	608	808
										WO	199	7 - t	JS13	383	1	W	199	708	06
OTHER SO	URCE	(S):			MARP	ΑT	130:	2674	54										

$$\mathbb{R}^{1}$$

$$\mathbb{R}^{2}$$

$$\mathbb{R}^{2}$$

$$\mathbb{R}^{2}$$

GI

AB Di-N-substituted piperazine or 1,4 di-substituted piperadine compds. [I; Y = CH, N, C6H5C, CH3C, (CH3)2CHC, etc.; Z = N; X = O, S, SO2, NMe, CO, CH2; R = (un)substituted phenyl; R1 = O, H2, Me and H, spiroheterocyclic; R2 = Me, H; R3 = 2-MeC6H4CO, COOEt, SO2CH2CH2CH3, COCF2CF3, etc.] (including all isomers, salts, esters, and solvates) are prepared as muscarinic antagonists useful for treating cognitive disorders such as Alzheimer's disease. Pharmaceutical compns. and methods of preparation are also disclosed. Also disclosed are synergistic combinations of compds. of the above formula with acetylcholinesterase inhibitors. Thus, compound II was prepared from (S)- α -methylbenzylamine and trifluoroacetic anhydride via 12 steps.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

1999:193839 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 130:252377

TITLE: Preparation of di-N-substituted piperazines or 1,4

disubstituted piperidines as muscarinic antagonists Lowe, Derek; Chang, Wei; Kozlowski, Joseph; Berger, Joel G.; Mcquade, Robert; Barnett, Allen; Sherlock, Margaret; Tom, Wing; Dugar, Sundeep; Chen, Lian-Yong; Clader, John W.; Chackalamannil, Samuel; Yuguang,

Wang; Mccombie, Stuart W.; Tagat, Jayaram R.; Vice, Susan F.; Vaccaro, Wayne; Green, Michael J.; Browne,

Margaret E.; Asberom, Theodros

PATENT ASSIGNEE(S):

Schering Corporation, USA

SOURCE:

U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 457,712,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

INVENTOR(S):

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5883096	Α	19990316	US 1996-602403	19960216
CA 2212895	· AA	19960829	CA 1996-2212895	19960216
TW 464646	В	20011121	TW 1996-85101945	19960216
ES 2215190	Т3	20041001	ES 1996-906286	19960216
ZA 9601293	Α	19960819	ZA 1996-1293	19960219
US 5889006	Α	19990330	US 1996-700628	19960808
US 6037352	Α	20000314	US 1998-195742	19981119
US 6043255	Α	20000328	US 1999-266079	19990310
US 6288068	B1	20010911	US 2000-482168	20000112
US 2002103205	A1	20020801	US 2001-902849	20010711
US 6498168	B2	20021224		
PRIORITY APPLN. INFO.:			US 1995-392697	B2 19950223
			US 1995-457712	B2 19950602
			US 1996-602403	A2 19960216
			US 1996-700628	A3 19960808
			US 1998-195742	A3 19981119
			US 2000-482168	A3 20000112

OTHER SOURCE(S): MARPAT 130:252377

GI

$$\begin{array}{c|c}
R^3 \\
R - X \\
\hline
R^2 1 \\
R^2 7 \\
R^2 7 \\
R^2 7
\end{array}$$

Di-N-substituted piperazines or 1,4-di-substituted piperidines I [one of Y and Z is N and the other is N, CH, or C-alkyl; X = 0, SOO-2, amino, substituted amino, CO, CH2, mono or disubstituted methylene, CS, CONR20, NR20SO2, NR20CO, SO2NR20, CH:CH, C.tplbond.C, NHC(O)NH; R = optionally substituted Ph, aryl, cycloalkyl; R1, R21 = H, CN or optionally substituted alkyl; R2 = optionally substituted cycloalkyl or piperidyl; R3, R4, R5, R20, R27, R28 are as defined in the specification], muscarinic antagonists, were prepared E.g., II was prepared

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:120328 HCAPLUS

DOCUMENT NUMBER: 130:296863

TITLE: Total Synthesis of (+)-Himbacine and (+)-Himbeline AUTHOR(S): Chackalamannil, Samuel; Davies, Robert J.; Wang,

Yuguang; Asberom, Theodros; Doller, Dario; Wong, Jesse; Leone, Daria; McPhail, Andrew T.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

SOURCE: Journal of Organic Chemistry (1999), 64(6), 1932-1940

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 130:296863

GI

^{*} STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Himbacine (I) (R = Me), a complex piperidine alkaloid isolated from the bark of Australian magnolias, is a promising lead in Alzheimer's disease research due to its potent muscarinic receptor antagonist property. The authors have described a highly efficient synthetic strategy that resulted in the total synthesis of I in about 10% overall yield and isohimbacine (II), an unnatural isomer of himbacine, in 18% overall yield. The total synthesis of himbacine was initially approached using an intramol. Diels-Alder reaction as the key step to generate intermediate (III) followed by a [3 + 2] cycloaddn. with nitrone (IV) to produce the isoxazolidine derivative (V). Methylation followed by catalytic reduction of V gave 12'-hydroxyhimbacine, which, upon dehydration, gave II as the sole product. In an alternative approach, an all-encompassing intramol. Diels-Alder reaction of an appropriately substituted tetraene derivative (VI), which bears the entire latent carbon framework and functional group substitution of himbacine, gave the desired advanced tricyclic intermediate, which was readily converted to (+)-himbeline (I) (R = H) (VII) and (+) - himbacine.

REFERENCE COUNT: THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:65892 HCAPLUS

DOCUMENT NUMBER: 128:140691

TITLE: Preparation of 1,4-disubstituted piperidines as

muscarinic antagonists

INVENTOR (S): Asberom, Theodros; Lowe, Derek B.; Green,

Michael J.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.							APPLICATION NO.						DATE					
WO	9801	425			A1		1998	0115		WO	19	97-1	JS11	176		1	9970	708
							BB,											
							LC,											
							SI,											
		AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM	[
	RW:	GH,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT	٠,	BE,	CH,	DE,	DK,	ES,	FI,	FR,
		GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE	;,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,
		GN,	ML,	MR,	ΝE,	SN,	TD,	TG										
CA	2259	655			AA		1998	0115		CA	19	97-2	2259	555		1:	9970	708
CA	2259	655			С		2003	0513										
	9735						1998	0202		AU	19	97-3	3581)		1:	9970	708
	7285				B2		2001											
	9125						1999	0506		EΡ	19	97-9	9323	21		1:	9970	708
EP	9125				В1		2002											
	R:					DK,	ES,	FR,	GB,	GR	.,	IT,	LI,	LU,	NL,	SE,	PT,	ΙE,
			LV,	FI,	RO													
	3335				Α		2000			NZ	19	97-3	3335	13		1:	9970	708
	3068				B2		2000		1	JP	19	98-5	5052	32		1	9970	708
	1151						1999											
	2277				E		2002									1		
	2182						2003			_						1	9970'	708
	9125						2003										9970	708
KR	2000	0235	99		Α		2000	0425		KR	19	99-1	70004	15		19	9990	107

PRIORITY APPLN. INFO.: US 1996-678618 A 19960710

WO 1997-US11176 W 19970708

OTHER SOURCE(S): MARPAT 128:140691

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The title compds. [I; X = a bond, O, S, etc.; R = C3-6 cycloalkyl, II, III, etc.; R1 = H, CN, CF3, etc.; R2 = cycloalkyl, cycloalkenyl, t-butoxycarbonyl, (un) substituted 4-piperidinyl; R3, R4 = H, halo, CF3, etc.; R5, R6 = H, alkyl, CF3, etc.], useful for treating cognitive disorders such as Alzheimer's disease, were prepared Compds. I are capable of enhancing acetylcholine (ACh) release with an ACh'ase inhibitors. Thus, a 5-step detailed synthesis of the title compound IV is described. The title compound V showed Ki of 40.8 nM against m2 receptor binding and of 66.4 nM against m4 receptor binding.

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 3 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

1997:162000 HCAPLUS ACCESSION NUMBER:

TITLE: Synthesis and biological evaluation of himbacine and

analogs.

AUTHOR (S): Chackalamannil, Samuel; Davies, Robert J.; Doller,

Dario; Wang, Yuguang; Asberom, Theodros;

Leone, Daria; McQuade, Robert; Ruperto, Vilma;

McPhail, Andrew T.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

Book of Abstracts, 213th ACS National Meeting, San SOURCE:

Francisco, April 13-17 (1997), MEDI-167. American

Chemical Society: Washington, D. C.

CODEN: 64AOAA

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

Himbacine (1) is a tetracyclic piperidine alkaloid isolated from the bark of the Australian pine tree of Galbulimima species. It has attracted considerable attention due to its promising biol. property as a selective muscarinic receptor antagonist. Enhancement of synaptic acetylcholine levels by selective inhibition of presynaptic muscarinic receptors is a promising therapeutic approach for the treatment of senile dementia associated with Alzheimer's disease. Himbacine is a potent inhibitor of the muscarinic receptor of M2 subtype with 10 to 20-fold selectivity toward other receptors. In the context of our efforts to develop potent and selective muscarinic receptor antagonists, we have developed a general and practical approach for the synthesis of himbacine analogs. We wish to report the syntheses of (+)-himbacine (1) and a number of its analogs using a highly convergent and practical approach. Addnl., a systematic evaluation of the structure-activity relationship and selectivity of these compds. against various muscarinic receptors will be presented.

L35 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:616758 HCAPLUS

DOCUMENT NUMBER: 126:8335

A Highly Efficient Total Synthesis of (+)-Himbacine TITLE:

AUTHOR (S): Chackalamannil, Samuel; Davies, Robert J.;

Asberom, Theodros; Doller, Dario; Leone, Daria

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,

07033, USA

SOURCE: Journal of the American Chemical Society (1996),

118(40), 9812-9813

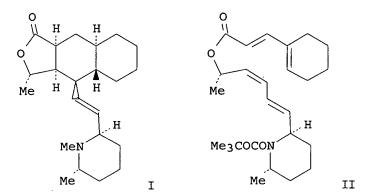
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 126:8335

GΙ



AB Himbacine (I) is a complex tetracyclic alkaloid isolated from the Australian pine tree of Galbulimima species. It is a potent muscarinic antagonist and, therefore, a promising therapeutic lead in the discovery of treatment for Alzheimer's disease. (+)-I has been synthesized in eleven linear steps from (S)-2-methylpiperidine.L-tartrate salt in 9.7% yield. The key step involves an all-encompassing, enantioselective intramol. Diels-Alder reaction of tetraene derivative II which bears the entire latent carbon framework and functional group substitution of I.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:414670 HCAPLUS

TITLE: Himbacine analogs as muscarinic receptor antagonists

AUTHOR(S): Doller, Dario; Chackalamannil, Samuel; Asberom,

Theodros; Leone, Daria

CORPORATE SOURCE: Chemistry Research, Schering-Plough Research

Institute, Kenilworth, NJ, 07033, USA

SOURCE: Book of Abstracts, 212th ACS National Meeting,

Orlando, FL, August 25-29 (1996), MEDI-082. American

Chemical Society: Washington, D. C.

CODEN: 63BFAF

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Himbacine, an alkaloid isolated from barks of trees of Galbulimima species, has long been recognized as a potential lead for the development of selective muscarinic receptor antagonists in Alzheimer desease studies. Despite its complex structure, remarkably its eight chiral centers, we have developed synthetic methods that allowed us to study the structure-activity relationship of himbacine analogs, all of which display the alkaloid's original tricycle moiety. We have examined the importance of the double bond, as well as other substituents, in the bridge region.

Also, substitution on the lactone ring and the nature of the basic unit were studied. As a result, we have demonstrated the crucial nature of the trans-6'-Me group in determining potencies and selectivities against muscarinic receptors. Modeling and exptl. results point towards the existence of key hydrophobic interactions between himbacine and the receptor near the basic site.

L35 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:255608 HCAPLUS

DOCUMENT NUMBER: 123:83224

TITLE: 4,5-bridged-2,3,4,5-tetrahydro-1H-3-benzazepine-7-ols

and derivatives and compositions and methods employing such compounds for the treatment of psychoses???, drug

dependence, D1 dependent neurol. disorder or pain

INVENTOR(S): Asberom, Theodros; O'Connor, Edward; Berger,

Joel G.; Clader, John W.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: U.S., 25 pp. Cont.-in-part of U.S. Ser. No.

474,428, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PAT	CENT	NO.			KINI)	DATE		7	APPL	ICAT	ION I	NO.		D	ATE	
	-					_									-		
US	5362	728			Α		1994	1108	1	US 1	992-	9157	10		1	9920'	729
WO	9111	437			A1		1991	8080	1	WO 1	991-	US50:	3		1:	9910	131
	W:	AU, SU,	-	BG,	BR,	CA,	FI,	HU,	JP,	KP,	KR,	LK,	MC,	MW,	NO,	RO,	SD,
	RW:	AT,	BE,		-		CG, SN.	-		DE,	DK,	ES,	FR,	GA∙,	GB,	GR,	IT,

PRIORITY APPLN. INFO.: US 1990-474428 B2 19900202

WO 1991-US503 W 19910131

OTHER SOURCE(S): MARPAT 123:83224

GI.

AB Novel benzazepines of the formula I or a pharmaceutically acceptable salt thereof, wherein R represents H, alkyl, allyl or cyclopropylmethyl; A represents [CR1R2]n; n represents 3 or 4; R1 and R2 may be the same or different and each independently represents H, OH, alkyl, alkoxy, Ph or substituted Ph, with the proviso that R1 and R2 on the same carbon atom are not both OH, or R1 and R2 on the same carbon atom together represent :O; G represents H, R3(CO) or ArNHCO; R3 represents H, alkyl, alkoxy, Ph or substituted phenyl; Ar represents Ph or substituted phenyl; and Y and Z may be the same or different and each is independently selected from H, halo, alkyl, alkoxy or haloalkyl; the pharmaceutically acceptable salts thereof, and pharmaceutical compns. thereof, useful in the treatment of

psychoses, drug dependence, D1 dependent neurol. disorder or pain are disclosed. Conditioned avoidance response test (min. ED mpk p.o.) in squirrel monkey: from 3 to >10; inhibition consts. Ki (nM) for D-1 receptor binding: from 2.8 to 335, compared to from 380 to >10,000 for the D-2 site. Pharmaceutical formulations were given.

L35 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:511485 HCAPLUS

DOCUMENT NUMBER: 117:111485

TITLE: Preparation of 4,5-cycloalkano-3-benzazepin-7-ols as

dopaminergic D1 antagonists

INVENTOR(S): Asberom, Theodros; O'Connor, Edward; Berger,

Joel Gilbert; Clader, John Welch

PATENT ASSIGNEE(S): Schering Corp., USA SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	TENT NO.					DATE		1	APP	LICAT	ION I	NO.		E	ATE	
	9111437 W: AU	, J, BB,		A1												
	RW: AT	J, US C, BE, J, ML,				•			DE	, DK,	ES,	FR,	GA,	GB,	GR,	IT,
CA	2075181		•	•		•	•		CA	1991-	2075	181		1	9910	131
CA	2075181			С		1997	1209									
EP	513174			A1		1992	1119	I	EΡ	1991-	9041	14		1	9910	131
EP	513174			B1		1995	0816		•							
	R: AT	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE		
JP	0550476	9		T2		1993	0722	į	JP	1991-	50444	42		1	9910	131
JP	0601347	4		B4		1994										
AU	646432			B2		1994	0224	1	UA	1991-	72432	2		1	9910	131
ES	2075429)		Т3		1995	1001	I	ES	1991-	9041:	14		1	9910	131
US	5362728	,		Α		1994	1108	τ	JS	1992-	9157	10		1	9920	729
FI	9203458	}		Α		1992	0731	I	FI	1992-	3458			1	9920	731
NO	9203042			Α		1992	1001	1	OV	1992-3	3042			1	9920	731
PRIORITY	APPLN.	INFO	. :					τ	JS	1990-4	47442	28	7	A 1	9900	202
	(-)							V	OW	1991-1	JS503	3	1	v 1	9910	131

OTHER SOURCE(S): MARPAT 117:111485

GI

AB Title compds. I [R = H, alkyl, allyl, cyclopropylmethyl; A = (CR1R2)n; n = 3, 4; R1, R2 = H, OH, alkyl, alkoxy, (substituted) Ph; R1 and R2 on the same C atom both \neq OH, or R1 and R2 on same C = O; G = H, R3CO, ArNHCO; R3 = H, alkyl, alkoxy, (substituted) Ph; Ar = (substituted) Ph; Y, Z = H, halo, alkyl, alkoxy, haloalkyl] were prepared as dopaminergic D1 antagonists useful as antipsychotics, analgesics, and for the treatment of drug dependence. Thus, alkylated amine II (preparation given) was cyclized in the presence of MeSO3H to give the cyclic enamine, which was reduced by NaCNBH3 to give I [Y = Cl; G = Me; A = (CH2)3; Z = H; R = H]. N-ethoxycarbonylation of the latter by ClCO2Et, followed by LiAlH4 reduction and ether cleavage by BBr3 gave title compound III. III had Ki of 2.8 nM against binding of 3H-Sch 23390 at dopaminergic D1 receptors. Formulations containing I were prepared

L35 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:20961 HCAPLUS

DOCUMENT NUMBER: 116:20961

TITLE: Preparation of 4,5-cycloalkano-3-benzazepin-7-ols as

nervous system agents.

INVENTOR (S): Asberom, Theodros; O'Connor, Edward; Berger,

Joel Gilbert; Clader, John Welch

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE ______ 19910808 WO 9111437 A1 WO 1991-US503 19910131 AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US

RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1990-464428 19900202

US 1990-474428 19900202

OTHER SOURCE(S): MARPAT 116:20961

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 A
 R^{40}
 N^{R}
 N^{R}
 N^{R}
 N^{R}
 N^{R}
 N^{R}
 N^{R}
 N^{R}

Title compds. [I; R = H, alkyl, allyl, cyclopropylmethyl; A = (CR1R2)n, R1, R2 = H, HO, alkyl, alkoxy, (substituted) Ph, R1, R2 on the same C \neq HO, R1, R2 on the same C = O; G = H, ArNHCO, Ar = (substituted) Ph, R3CO, R3 = H, alkyl, alkoxy, (substituted) Ph; Y, Z = H, halo, alkyl, alkoxy, haloalkyl; n = 3,4] useful for treating psychoses, drug dependence, D1 dependent neurol. disorder or pain, are prepared Benzoxazine II (R4 = Me) (preparation from cyclopentanone and 5-bromo-2-chloroanisole given), in CH2Cl2 at -78° was treated with BBr3; the reaction mixture was stirred at -78° for 1 h, then at room temperature for 2 h to give II [R4 = H]. I showed biol. activity (e.g., suppression of conditioned avoidance in squirrel monkeys) for treating the mentioned disorders. Capsule and tablet formulations are given.

L35 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1991:535752 HCAPLUS

DOCUMENT NUMBER:

115:135752

TITLE:

The chemistry of cyclic vinyl ethers. 6. Total synthesis of polyether ionophore antibiotics of the

calcimycin (A-23187) class

AUTHOR (S):

SOURCE:

Boeckman, Robert K., Jr.; Charette, Andre B.;

Asberom, Theodros; Johnston, Brian H.

CORPORATE SOURCE:

Dep. Chem., Univ. Rochester, Rochester, NY, 14627, USA

Journal of the American Chemical Society (1991),

113(14), 5337-53

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 115:135752

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB An extremely convergent (longest linear sequence 16 steps), stereoselective, and potentially general synthesis of the antibiotic ionophores was devised. The key steps involve a coupling reaction between the chiral nonracemic subunits dihydropyran I (as the α -lithio anion) and bromide II. Subsequent acid-promoted cyclization directly produces the spirocyclic ring system found in the ionophore X-14885A (III; R = H, R1 = OH). Alternatively, cyclopropanation of substituted vinyl

ether IV followed by acid treatment afforded the spiroketal V that was subsequently converted into the polyether ionophore calcimycin (III; R = Me, R1 = NHMe) and also Cezomycin (III; R = Me, R1 = H).

L35 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1988:5753 HCAPLUS

DOCUMENT NUMBER:

108:5753

TITLE:

A convergent general synthetic protocol for construction of spirocyclic ketal ionophores: an application to the total synthesis of (-)-A-23187

(calcimycin)

AUTHOR (S):

Boeckman, Robert K., Jr.; Charette, Andre B.;

Asberom, Theodros; Johnston, Brian H.

CORPORATE SOURCE:

Dep. Chem., Univ. Rochester, Rochester, NY, 14627, USA

SOURCE:

Journal of the American Chemical Society (1987),

109(24), 7553-5

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: LANGUAGE:

Journal English

OTHER SOURCE(S):

CASREACT 108:5753

GI

AB A flexible and efficient synthetic strategy for the synthesis of calcimycin (I) is detailed. Coupling of the anion derived from a suitably substituted dihydropyran with an appropriately substituted bromide followed by cyclopropanation and cyclization of the resulting cyclopropyl ethers provides a key, differentially protected, spiroketal which was elaborated to I. Overall, the route is highly convergent and efficient (13 steps along the longest sequence), and readily lends itself to the preparation of related ionophores and analogs thereof.

Ι

L35 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1986:533632 HCAPLUS

DOCUMENT NUMBER:

105:133632

TITLE:

Application of cyclic vinyl ether carbanions: progress towards enantioselective synthesis of

calcimycin

AUTHOR (S):

Asberom, Theodros

CORPORATE SOURCE:

Univ. Rochester, Rochester, NY, USA

SOURCE:

(1985) 244 pp. Avail.: Univ. Microfilms Int., Order

No. DA8516459

From: Diss. Abstr. Int. B 1986, 46(6), 1918

DOCUMENT TYPE:

Dissertation

LANGUAGE:

English

AB Unavailable

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=> => d stat que nos
L4
                STR
L10
                STR
L12
          25437 SEA FILE=REGISTRY SSS FUL L4 AND L10
L13
                STR
L15
              5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13
              3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15
L16
L17
          25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15
            183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE
L18
           3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L19
           2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?
L20
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L21
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L23
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L25
L29
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L31
                                                 L29 AND L25
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             40 SEA FILE=HCAPLUS ABB=ON PLU=ON ("JOSIEN H"/AU OR "JOSIEN H
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                B"/AU OR "JOSIEN HUBERT"/AU OR "JOSIEN HUBERT B"/AU) NOT (L16
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L35
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                W"/AU OR ("HOBBS DOUG W"/AU OR "HOBBS DOUGLAS"/AU) OR ("HOBBS
                DOUGLAS W"/AU OR "HOBBS DOUGLAS WALSH"/AU)) NOT (L16 OR L22 OR
                L32 OR L34 OR L35)
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L37
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=> d ibib abs hitstr 137 1-7
L37 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                         2004:981365 HCAPLUS
DOCUMENT NUMBER:
                         141:379943
TITLE:
                         Preparation of pyrazolopyrimidines as cyclin-dependent
                         kinase inhibitors
INVENTOR(S):
                         Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.;
                         Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Mallams,
                         Alan; Alvarez, Carmen S.; Keertikar, Kartik M.;
                         Rivera, Jocelyn; Chan, Tin-Yau; Madison, Vincent;
                         Fischmann, Thierry O.; Dillard, Lawrence W.; Tran,
                         Vinh D.; He, Zhen Min; James, Ray Anthony; Park,
                         Haengsoon; Paradkar, Vidyadhar M.; Hobbs, Douglas
                         Walsh
PATENT ASSIGNEE(S):
                         Schering Corporation, USA; Pharmacopeia, Inc.
SOURCE:
                         U.S. Pat. Appl. Publ., 1044 pp., Cont.-in-part of U.S.
                         Ser. No. 654,546.
                         CODEN: USXXCO
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				-	
US 2004209878	A1	20041021	US 2004-776988		20040211
US 2004209878	A1	20041021	US 2004-776988		20040211
PRIORITY APPLN. INFO.:			US 2002-408027P	P	20020904
			US 2002-421959P	P	20021029
			US 2003-654546	A2	20030903
			US 2004-776988	Α	20040211

GI

AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020 μ M and 0.029 μ M against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a Part

III of I-III series.

IT 677278-60-3P 677278-83-0P 677278-88-5P 677281-50-4P 677281-71-9P 677281-76-4P 677285-84-6P 677286-62-3P 677287-60-4P 677289-03-1P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors

for treating cancer)

RN 677278-60-3 HCAPLUS CN 4-Piperidinamine, N-

4-Piperidinamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677278-83-0 HCAPLUS

CN 4-Piperidinamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677278-88-5 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[4-[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-

a]pyrimidin-7-yl]amino]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677281-50-4 HCAPLUS

CN 3-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677281-71-9 HCAPLUS

CN 3-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-(9CI) (CA INDEX NAME)

RN677281-76-4 HCAPLUS

2-Thiophenecarboxylic acid, 3-[[3-[[[3-bromo-5-(2-CN chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]methyl]-1piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN

677285-84-6 HCAPLUS 1H-Pyrrole, 2-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677286-62-3 HCAPLUS

CN 1H-Pyrrole, 2-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677287-60-4 HCAPLUS

CN 1H-Pyrrole, 2-[[4-[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

677289-03-1 HCAPLUS RN

1H-Pyrrole, 2-[[3-[[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-CNyl]amino]methyl]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

HCAPLUS COPYRIGHT 2005 ACS on STN L37 ANSWER 2 OF 7

2004:980998 HCAPLUS ACCESSION NUMBER:

141:379942 DOCUMENT NUMBER:

Preparation of pyrazolopyrimidines as cyclin-dependent TITLE:

kinase inhibitors

INVENTOR (S):

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Rivera, Jocelyn; Chan, Tin-Yau; Madison, Vincent; Fischmann, Thierry O.; Dillard, Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray Anthony; Park, Haengsoon; Paradkar, Vidyadhar M.; Hobbs, Douglas Walsh

PATENT ASSIGNEE(S):

SOURCE:

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PATENT INFORMATION:

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PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004209878	A 1	20041021	US 2004-776988		20040211
US 2004209878	A1	20041021	US 2004-776988		20040211
PRIORITY APPLN. INFO.:			US 2002-408027P	P	20020904
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			US 2003-654546	A2	20030903
			US 2004-776988	Α	20040211

GΙ

AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with

4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020 μ M and 0.029 μ M against CDK2 kinase (cyclin A or cyclin E-dependent). The

pharmaceutical composition comprising the compound I is claimed. This is a Part II of I-III series. TΤ 677793-40-7P 677793-41-8P 677793-42-9P 677793-43-0P 677793-44-1P 677793-45-2P 677793-47-4P 677793-48-5P 677793-49-6P 677793-50-9P 677793-51-0P 677793-52-1P 677793-53-2P 677793-54-3P 677793-55-4P 677793-56-5P 677793-57-6P 677793-58-7P 677793-59-8P 677793-60-1P 677793-61-2P 677793-62-3P 677793-63-4P 677793-64-5P 677793-65-6P 677793-66-7P 677793-67-8P 677793-68-9P 677793-69-0P 677793-70-3P 677793-71-4P 677793-72-5P 677793-73-6P 677793-74-7P 677793-75-8P 677793-76-9P 677793-77-0P 677793-78-1P 677793-79-2P 677793-80-5P 677793-81-6P 677793-82-7P 677793-83-8P 677793-84-9P 677793-85-0P 677793-86-1P 677793-87-2P 677793-88-3P 677793-89-4P 677793-90-7P 677793-91-8P 677793-92-9P 677793-93-0P 677793-94-1P 677793-95-2P 677793-96-3P 677793-97-4P 677793-98-5P 677793-99-6P 677794-00-2P 677794-01-3P 677794-02-4P 677794-03-5P 677794-04-6P 677794-05-7P 677794-06-8P 677794-07-9P 677794-08-0P 677794-09-1P · 677794-10-4P 677794-12-6P 677794-13-7P 677794-14-8P 677794-15-9P 677794-16-0P 677794-17-1P 677794-18-2P 677794-19-3P 677794-20-6P 677794-21-7P 677794-22-8P 677794-23-9P 677794-24-0P 677794-25-1P 677794-26-2P 677794-27-3P 677794-28-4P 677794-29-5P 677794-30-8P 677794-31-9P 677794-32-0P 677794-33-1P 677794-34-2P 677794-35-3P 677794-36-4P 677794-37-5P 677794-38-6P 677794-39-7P 677794-40-0P 677794-41-1P 677794-42-2P 677794-43-3P 677794-44-4P 677794-45-5P 677794-46-6P 677794-47-7P 677794-48-8P 677794-49-9P 677794-50-2P 677794-51-3P 677794-52-4P 677795-96-9P 677796-21-3P 677796-25-7P RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses) (preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors) RN677793-40-7 HCAPLUS Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

RN677793-41-8 HCAPLUS Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677793-42-9 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN · 677793-43-0 HCAPLUS CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

- RN 677793-44-1 HCAPLUS
- CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

- RN 677793-45-2 HCAPLUS
- CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-47-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-48-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-49-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

- RN 677793-50-9 HCAPLUS
- CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

- RN 677793-51-0 HCAPLUS
- CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-2-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-52-1 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5- \cdot CN a]pyrimidin-5-yl]-1-[[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN

677793-53-2 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677793-54-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-55-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-56-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-57-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-58-7 HCAPLUS

CN Benzenepropanoic acid, 4-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo [1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677793-59-8 HCAPLUS

CN Isoquinoline, 7-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)

RN 677793-60-1 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677793-61-2 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-62-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-63-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677793-64-5 HCAPLUS

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa)pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677793-65-6 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-66-7 HCAPLUS

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677793-67-8 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677793-68-9 HCAPLUS

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-69-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-70-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-71-4 HCAPLUS

Ward 10_663042-inventor search

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-72-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-73-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-74-7 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

RN677793-75-8 HCAPLUS

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX CNNAME)

Ward 10_663042-inventor search

RN 677793-76-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-(9CI) (CA INDEX NAME)

RN 677793-77-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-78-1 HCAPLUS

CN Benzoic acid, 2-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677793-79-2 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-80-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-81-6 HCAPLUS
CN 2-Thiophenecarboxylic acid, 3-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677793-82-7 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CFINDEX NAME)

RN 677793-83-8 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-

a]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-84-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Ward 10 663042-inventor search

RN

677793-85-0 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677793-86-1 HCAPLUS

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677793-87-2 HCAPLUS

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-88-3 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(3,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-89-4 HCAPLUS RN

CNPiperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Ward 10_663042-inventor search

RN 677793-90-7 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5a]pyrimidin-5-yl]-1-[(2,5-dichloro-3-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677793-91-8 HCAPLUS

Piperidine, 1-([1,1'-biphenyl]-4-ylsulfonyl)-4-[3-bromo-7-[(3-CNpyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN

677793-92-9 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[[2-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-93-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-94-1 HCAPLUS

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

677793-95-2 HCAPLUS
Piperidine, 1-[(4-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-CNpyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN677793-96-3 HCAPLUS

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-97-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-98-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3,4-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-99-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-00-2 HCAPLUS
Piperidine, 1-[(5-bromo-6-chloro-3-pyridinyl)sulfonyl]-4-[3-bromo-7-[(3-CNpyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX

RN

677794-01-3 HCAPLUS
Piperidine, 1-[[3,5-bis(trifluoromethyl)phenyl]sulfonyl]-4-[3-bromo-7-[(3-CN pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

Ward 10 663042-inventor search

677794-02-4 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-03-5 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

RN

677794-04-6 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-05-7 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME) CN

RN

677794-06-8 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME) CN

RN677794-07-9 HCAPLUS CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-08-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-09-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-10-4 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-12-6 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-13-7 HCAPLUS

Ward 10_663042-inventor search

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-14-8 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-15-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677794-16-0 HCAPLUS Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-17-1 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME) CN

RN677794-18-2 HCAPLUS

Ward 10_663042-inventor search

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

- RN 677794-19-3 HCAPLUS
- CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

- RN 677794-20-6 HCAPLUS
- CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677794-21-7 HCAPLUS Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN

a]pyrimidin-5-yl]-1-[(3,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-22-8 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(3,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-23-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-2-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-24-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-25-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677794-26-2 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

Ward 10 663042-inventor search

677794-27-3 HCAPLUS RNPiperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-28-4 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-RN CN

a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-(9CI) (CA INDEX NAME)

RN

677794-29-5 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) INDEX NAME)

RN 677794-30-8 HCAPLUS

CN Benzoic acid, 2-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677794-31-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-32-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-33-1 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677794-34-2 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-35-3 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

677794-36-4 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-37-5 HCAPLUS

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2,3-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Ward 10_663042-inventor search

RN 677794-38-6 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-39-7 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-40-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-41-1 HCAPLUS

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-42-2 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-chloro-2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-43-3 HCAPLUS
Piperidine, 1-([1,1'-biphenyl]-4-ylsulfonyl)-3-[3-bromo-7-[(3-CN pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX

RN

677794-44-4 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-45-5 HCAPLUS

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN 677794-46-6 HCAPLUS

CN Piperidine, 1-[(4-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN 677794-47-7 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-48-8 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Ward 10_663042-inventor search

RN 677794-49-9 HCAPLUS

CN Benzenepropanoic acid, 4-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo [1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} O \\ \parallel \\ MeO-C-CH_2-CH_2 \\ \hline \\ O \\ \hline \\ S-N \\ \hline \\ N-N \\ \hline \\ NH \\ \hline \\ CH_2 \\ \hline \\ N \\ \end{array}$$

RN 677794-50-2 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-51-3 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-52-4 HCAPLUS

CN Isoquinoline, 7-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)

$$F_3C-C$$

$$0$$

$$N$$

$$N$$

$$N$$

$$N$$

$$CH_2$$

RN 677795-96-9 HCAPLUS

CN 4-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

677796-21-3 HCAPLUS RN

4-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-(9CI) (CA INDEX NAME) CN

PAGE 1-A

PAGE 2-A

RN 677796-25-7 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[4-[[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]methyl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

Cl

L37 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:265849 HCAPLUS

DOCUMENT NUMBER:

140:321371

TITLE:

Preparation of pyrazolopyrimidines as cyclin-dependent

kinase inhibitors

INVENTOR(S):

Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Doll, Ronald J.; Girijavallabhan, Viyyoor Moopil; Mallams, Alan; Alvarez, Carmen S.; Keertikar, Kartik

M.; Rivera, Jocelyn; Chan, Tin-yau; Madison, Vincent; Fischmann, Thierry O.; Dillard, Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray Anthony; Park, Haengsoon; Paradkar, Vidyadhar M.; Hobbs, Douglas Walsh

PATENT ASSIGNEE(S): SOURCE:

Schering Corporation, USA PCT Int. Appl., 609 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

GΙ

Patent English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PAT	KIND DATE				APPLICATION NO.						DATE						
WO	0 2004022561					A1 20040318			1	WO 2	003-		20030903				
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	HR,	HU,
		ID,	IL,	IN,	IS,	JP,	KG,	KR,	ΚZ,	LC,	LK,	LR,	LT,	LU,	LV,	MA,	MD,
		MG,	MK,	MN,	MX,	NI,	NO,	NZ,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SE,	SG,
		SK,	SL,	SY,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UZ,	VC,	VN,	YU,	ZA,	ZM,
		AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM							
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	BE,	BG,
		CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HU,	ΙE,	ΙΤ,	LU,	MC,
		NL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,
		GW,	ML,	MR,	ΝE,	SN,	TD,	TG									
PRIORITY APPLN. INFO.:									US 2002-408027P						P 20020904		
US 2002-421959P P 2002												0021	029				

$$\mathbb{R}^{2}$$
 \mathbb{R}^{4}
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AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020 μM and 0.029 μM against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a Part

III of I-III series.

TT 677278-60-3P 677278-83-0P 677278-88-5P 677281-50-4P 677281-71-9P 677281-76-4P 677285-84-6P 677286-62-3P 677287-60-4P 677289-03-1P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors for treating cancer)

RN 677278-60-3 HCAPLUS

CN 4-Piperidinamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677278-83-0 HCAPLUS

CN 4-Piperidinamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677278-88-5 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[4-[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677281-50-4 HCAPLUS

CN 3-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677281-71-9 HCAPLUS

CN 3-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-(9CI) (CA INDEX NAME)

RN 677281-76-4 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[3-[[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]methyl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN

677285-84-6 HCAPLUS
1H-Pyrrole, 2-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA

RN

677286-62-3 HCAPLUS
1H-Pyrrole, 2-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

RN677287-60-4 HCAPLUS

1H-Pyrrole, 2-[[4-[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME) CN

RN

677289-03-1 HCAPLUS 1H-Pyrrole, 2-[[3-[[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-CNyl]amino]methyl]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

L37 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:265847 HCAPLUS

DOCUMENT NUMBER:

140:321370

TITLE:

Preparation of pyrazolopyrimidines as cyclin-dependent

kinase inhibitors

INVENTOR(S):

Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Doll, Ronald J.; Girijavallabhan, Viyyoor Moopil; Mallams, Alan; Alvarez, Carmen S.; Keertikar, Kartik M.; Rivera, Jocelyn; Chan, Tin-yau; Madison, Vincent; Fischmann, Thierry O.; Dillard, Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray Anthony; Park, Haengsoon; Paradkar, Vidyadhar M.; Hobbs, Douglas

Walsh

PATENT ASSIGNEE(S):

SOURCE:

Schering Corporation, USA PCT Int. Appl., 609 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.						KIND DATE			APPLICATION NO.						DATE			
WO	2004	0225	61		A1	A1 20040318			WO 2003-XA27555						20030903				
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,		
		CO,	CR,	CZ,	DĒ,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	HR,	HU,		
		ID,	IL,	IN,	IS,	JP,	KG,	KR,	KZ,	LC,	LK,	LR,	LT,	LU,	LV,	MA,	MD,		
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		SK,	SL,	SY,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UΖ,	VC,	VN,	YU,	ZA,	ZM,		
		AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ΤJ,	TM									
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		CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,		
		NL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,		
		GW,	ML,	MR,	ΝE,	SN,	TD,	TG											
PRIORITY					•	US 2002-408027P						P 20020904							
									•	US 2	002-	4219	59P]	P 20021029				

GI

AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020 μM and 0.029 μM against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a

Part

II of I-III series. IT 677793-40-7P 677793-41-8P 677793-42-9P 677793-43-0P 677793-44-1P 677793-45-2P 677793-47-4P 677793-48-5P 677793-49-6P 677793-50-9P 677793-51-0P 677793-52-1P 677793-53-2P 677793-54-3P 677793-55-4P 677793-56-5P 677793-57-6P 677793-58-7P 677793-59-8P 677793-60-1P 677793-61-2P 677793-62-3P 677793-63-4P 677793-64-5P 677793-65-6P 677793-66-7P 677793-67-8P 677793-68-9P 677793-69-0P 677793-70-3P 677793-71-4P 677793-72-5P 677793-73-6P 677793-74-7P 677793-75-8P 677793-76-9P 677793-77-0P 677793-78-1P 677793-79-2P 677793-80-5P 677793-81-6P 677793-82-7P 677793-83-8P 677793-84-9P 677793-85-0P 677793-86-1P 677793-87-2P 677793-88-3P 677793-89-4P 677793-90-7P 677793-91-8P 677793-92-9P 677793-93-0P 677793-94-1P 677793-95-2P 677793-96-3P 677793-97-4P

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677793-98-5P 677793-99-6P 677794-00-2P
677794-01-3P 677794-02-4P 677794-03-5P
677794-04-6P 677794-05-7P 677794-06-8P
677794-07-9P 677794-08-0P 677794-09-1P
677794-10-4P 677794-12-6P 677794-13-7P
677794-14-8P 677794-15-9P 677794-16-0P
677794-17-1P 677794-18-2P 677794-19-3P
677794-20-6P 677794-21-7P 677794-22-8P
677794-23-9P 677794-24-0P 677794-25-1P
677794-26-2P 677794-27-3P 677794-28-4P
677794-29-5P 677794-30-8P 677794-31-9P
677794-32-0P 677794-33-1P 677794-34-2P
677794-35-3P 677794-36-4P 677794-37-5P
677794-38-6P 677794-39-7P 677794-40-0P
677794-41-1P 677794-42-2P 677794-43-3P
677794-44-4P 677794-45-5P 677794-46-6P
677794-47-7P 677794-48-8P 677794-49-9P
677794-50-2P 677794-51-3P 677794-52-4P
677795-96-9P 677796-21-3P 677796-25-7P
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU
(Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study);
PREP (Preparation); USES (Uses)
   (preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors)
677793-40-7 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-
a]pyrimidin-5-yl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)
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RN CN

RN 677793-41-8 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-42-9 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-43-0 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-44-1 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(3-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677793-45-2 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(4-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-47-4 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-48-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-49-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-50-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-51-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-2-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-52-1 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

677793-53-2 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-RN CN a]pyrimidin-5-yl]-1-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

RN

677793-54-3 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) CN(CA INDEX NAME)

RN 677793-55-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-56-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-57-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-58-7 HCAPLUS

CN Benzenepropanoic acid, 4-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo [1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & & & & & & Br \\ MeO-C-CH_2-CH_2 & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

RN 677793-59-8 HCAPLUS

CN Isoquinoline, 7-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)

$$F_3C-C$$

$$0$$

$$0$$

$$NH$$

$$0$$

$$CH_2$$

RN 677793-60-1 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677793-61-2 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-62-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-63-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-64-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-65-6 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME) CN

RN

677793-66-7 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME) CN

677793-67-8 HCAPLUS RN

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-68-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-69-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-70-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-71-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-72-5 HCAPLUS

RN

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-73-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-74-7 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677793-75-8 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-76-9 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-(9CI) (CA INDEX NAME)

RN 677793-77-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-78-1 HCAPLUS

CN Benzoic acid, 2-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN

677793-79-2 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677793-80-5 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a)pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-81-6 HCAPLUS
CN 2-Thiophenecarboxylic acid, 3-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677793-82-7 HCAPLUS
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

677793-83-8 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) CN(CA INDEX NAME)

RN

677793-84-9 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME) CN

RN 677793-85-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-86-1 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-87-2 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677793-88-3 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(3,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677793-89-4 HCAPLUS
Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) CN (CA INDEX NAME)

RN 677793-90-7 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dichloro-3-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-91-8 HCAPLUS

CN Piperidine, 1-([1,1'-biphenyl]-4-ylsulfonyl)-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN 677793-92-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-93-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-94-1 HCAPLUS

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN 677793-95-2 HCAPLUS

CN Piperidine, 1-[(4-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN 677793-96-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-97-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-98-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3,4-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677793-99-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-00-2 HCAPLUS
Piperidine, 1-[(5-bromo-6-chloro-3-pyridinyl)sulfonyl]-4-[3-bromo-7-[(3-CN pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN677794-01-3 HCAPLUS

Piperidine, 1-[[3,5-bis(trifluoromethyl)phenyl]sulfonyl]-4-[3-bromo-7-[(3-CN pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

677794-02-4 HCAPLUS RN

Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-ÇN a]pyrimidin-5-yl]-1-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX

RN

677794-03-5 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

RN

677794-04-6 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-05-7 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-06-8 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677794-07-9 HCAPLUS

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-08-0 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-09-1 HCAPLUS RN

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-10-4 HCAPLUS RN

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-12-6 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN677794-13-7 HCAPLUS

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-14-8 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-15-9 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-16-0 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-17-1 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-18-2 HCAPLUS

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-19-3 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-20-6 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

677794-21-7 HCAPLUS RN

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(3,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-22-8 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(3,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-23-9 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(5-chloro-2-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-24-0 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

677794-25-1 HCAPLUS RN

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

RN

677794-26-2 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

RN 677794-27-3 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-28-4 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl](9CI) (CA INDEX NAME)

RN 677794-29-5 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) (CAINDEX NAME)

RN 677794-30-8 HCAPLUS

CN Benzoic acid, 2-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677794-31-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-32-0 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX

677794-33-1 HCAPLUS RN

2-Thiophenecarboxylic acid, 3-[[3-[3-bromo-7-[(3-CNpyridinylmethyl) amino] pyrazolo[1,5-a] pyrimidin-5-yl] -1piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 677794-34-2 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-35-3 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-36-4 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-37-5 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-38-6 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-39-7 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-40-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-41-1 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-42-2 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chloro-2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN

CNpyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX

RN

677794-44-4 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CNa]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN

677794-45-5 HCAPLUS
Piperidine, 1-[(2-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-b CN pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

RN

677794-46-6 HCAPLUS
Piperidine, 1-[(4-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX CNNAME)

RN 677794-47-7 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-48-8 HCAPLUS
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

677794-49-9 HCAPLUS RN

Benzenepropanoic acid, 4-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo CN[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} O \\ \parallel \\ MeO-C-CH_2-CH_2 \\ \hline \\ O \\ \hline \\ S \\ \hline \\ N \\ \hline \\ N \\ \end{array}$$

RN

677794-50-2 HCAPLUS
Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME) CN

677794-51-3 HCAPLUS RN

Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-CN a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 677794-52-4 HCAPLUS

CN Isoquinoline, 7-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)

RN 677795-96-9 HCAPLUS

CN 4-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

677796-21-3 HCAPLUS RN

4-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-(9CI) (CA INDEX NAME) CN

PAGE 1-A

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677796-25-7 HCAPLUS RN

2-Thiophenecarboxylic acid, 3-[[4-[[[3-bromo-5-(2-CNchlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]methyl]-1piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

L37 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:613831 HCAPLUS

DOCUMENT NUMBER: 127:278203

TITLE: Benzoxazinone and benzopyrimidinone piperidinyl

tocolytic oxytocin receptor antagonists

Bock, Mark G.; Evans, Ben E.; Williams, Peter D.; Freidinger, Roger M.; Pettibone, Douglas J.; INVENTOR(S):

Hobbs, Doug W.; Anderson, Paul S.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: U.S., 140 pp., Cont.-in-part of U.S. Ser. No. 92,840,

abandoned.
CODEN: USXXAM

CODEN: USXXAI

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
US 5665719 A 19970909 US 1995-470693 19950606
PRIORITY APPLN. INFO.: US 1993-92840 B2 19930716

OTHER SOURCE(S): MARPAT 127:278203

GΙ

- * STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY AVAILABLE VIA OFFLINE PRINT *
- Compds. of formula I [X = O, NH, or NR8; Y = CH2, CHR8, or C(R8)2; R1 = AΒ camphor-10-yl, alkoxy, styryl, hydroxystyryl, furyl, (un) substituted thienyl, naphthyl, indolyl, tetrahydronaphthyl, (un) substituted pyridyl, pyrazinyl, (un) substituted cyclohexyl or Ph; R2 = H, alkoxy, alkyl, amino, alkylcarbonylamino, nitro, or halo; R3 = H, alkoxycarbonyl, cyano, or carbamoyl; and m = 0 or 1] and various analogs are disclosed. The compds. as useful as oxytocin (OT) and vasopressin receptor antagonists. Over 275 synthetic examples are given. For instance, Me 2,4-dihydroxybenzoate underwent Mitsunobu etherification with N-(tert-butoxycarbonyl)-4piperidinol (51%), followed by O-methylation of the remaining hydroxyl (88%), saponification of the Me ester (95%), and coupling of the resultant acid with 1-(4-piperidinyl)-1,2-dihydro-4H-3,1-benzoxazin-2-one (HCl salt) using EDC and HOBt (88%), to give title compound II [R = CO2Bu-tert]. latter was deprotected with HCl in dioxane (93%) and acetylated with Ac20 (89%) to give title compound II [R = Ac]. The latter inhibited binding of [3H]-OT to rat uterine OT receptors in vitro with an IC50 of 47 nM.
- IT 162043-19-8P 162044-15-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT

(Reactant or reagent); USES (Uses)

(preparation of benzoxazinone and benzopyrimidinone derivs. as oxytocin and vasopressin receptor antagonists)

RN 162043-19-8 HCAPLUS

Piperidine, 1-[2-methoxy-4-[[1-[[1-(phenylmethyl)-3-pyrrolidinyl]sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI)
(CA INDEX NAME)

PAGE 1-A

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162044-15-7 HCAPLUS RN1-Piperazinecarboxylic acid, 4-[[4-[3-methoxy-4-[[4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-1-piperidinyl]carbonyl]phenoxy]-1-piperidinyl]sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME) CN

PAGE 2-A

162043-21-2 HCAPLUS RN

Piperidine, 1-[4-[[1-[(1-ethyl-3-pyrrolidinyl)sulfonyl]-4-piperidinyl]oxy]-2-methoxybenzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, monohydrochloride CN(9CI) (CA INDEX NAME)

PAGE 1-A

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● HCl

RN

162044-10-2 HCAPLUS
Piperidine, 1-[2-methoxy-4-[[1-[(1-methyl-3-pyrrolidinyl)sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, monohydrochloride (9CI) (CA INDEX NAME) CN

PAGE 2-A

HCl

RN 162044-11-3 HCAPLUS
CN Piperidine, 1-[2-methoxy-4-[[1-[[1-[(2-methyl-3-pyridinyl)methyl]-3-pyrrolidinyl]sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 2-A

●2 HCl

RN 162044-17-9 HCAPLUS
CN Piperidine, 1-[2-methoxy-4-[[1-[[4-[(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 162044-18-0 HCAPLUS
CN Piperidine, 1-[2-methoxy-4-[[1-[(4-methyl-1-piperazinyl)sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, hydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

●x HCl

RN

162044-19-1 HCAPLUS
Piperidine, 1-[4-[[1-[(4-ethyl-1-piperazinyl)sulfonyl]-4-piperidinyl]oxy]-2-methoxybenzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, hydrochloride CN(9CI) (CA INDEX NAME)

PAGE 2-A

●x HCl

RN 196793-98-3 HCAPLUS
CN Piperidine, 1-[4-[[1-[(1-ethyl-3-pyrrolidinyl)sulfonyl]-4-piperidinyl]oxy]2-methoxybenzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI) (CA INDEX NAME)

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RN

196794-19-1 HCAPLUS
Piperidine, 1-[2-methoxy-4-[[1-[(1-methyl-3-pyrrolidinyl)sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI) (CA CNINDEX NAME)

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196794-20-4 HCAPLUS
Piperidine, 1-[2-methoxy-4-[[1-[[1-[(2-methyl-3-pyridinyl)methyl]-3-pyrrolidinyl]sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI) (CA INDEX NAME) RNCN

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RN 196794-23-7 HCAPLUS

CN Piperidine, 1-[2-methoxy-4-[[1-[[4-[(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI) (CA INDEX NAME)

PAGE 2-A

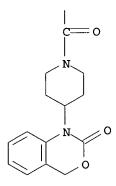
RN 196794-24-8 HCAPLUS
CN Piperidine, 1-[2-methoxy-4-[[1-[(4-methyl-1-piperazinyl)sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI) (CA INDEX NAME)

PAGE 2-A

RN

196794-25-9 HCAPLUS
Piperidine, 1-[4-[[1-[(4-ethyl-1-piperazinyl)sulfonyl]-4-piperidinyl]oxy]-2-methoxybenzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI) (CA INDEX CNNAME)

PAGE 2-A



L37 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

1995:470323 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 123:276051

Benzoxazinone and benzopyrimidinone piperidinyl TITLE:

tocolytic oxytocin receptor antagonists

INVENTOR(S):

Bock, Mark G.; Evans, Ben E.; Hobbs, Doug W.; Williams, Peter D.; Anderson, Paul S.; Freidinger,

Roger M.; Pettibone, Douglas J. Merck and Co., Inc., USA

PATENT ASSIGNEE(S):

PCT Int. Appl., 385 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PA	PATENT NO.							APPLICATION NO.						DATE			
WO	9502						1995	0126		WO 1	L994-	US77	84		1	 9940	 714
	W:	AM,	AU,	BB,	BG,	BR,	BY,	CA,	CN,	CZ,	FI,	GE,	HU,	JP,	ΚE,	KG,	KR,
		ΚZ,	LK,	LT,	LV,	MD,	MG,	MN,	MW,	NO,	NZ,	PL,	RO,	RU,	SD,	SI,	SK,
		TJ,	TT,	UA,	US,	UZ							•				
	RW:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	ML,	MR,	ΝE,	SN,	TD,	TG		
CA	2166	975			AA		1995	0126		CA 1	L994 -	2166	975		1	9940	714
	2166							-							•		
AU	9475	132			A1		1995	0213	;	AU 1	1994 -	7513	2		1	9940	714
	6918:						1998										
EP	7142	99			A1		1996	0605		EP 1	L994 -	9250	92		1	9940	714
EP	7142	99			В1		2002	0424									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IE,	ΙT,	LI,	LU,	NL,	PT,	SE
JP	0950	0134			T2		1997	0107		JP 1	L994-	5046	56		1	9940	714
AT	2165	80			E		2002	0515		AT 1	L994-	9250	92		1	9940	714
PRIORITY	Y APP	LN.	INFO	. :						US 1	L993-	9284	0 ·	1	A 1	9930	716
										WO 1	L994 -	US77	84	1	W 1	9940	714
OTHER SO	OURCE	(S):			MAR	PAT	123:	2760!	51								

AB Fused N-containing heterocyclic ring system derivs. I [A completes a 5- or 6-membered carbocyclic or N- and/or S-containing heterocyclic ring; X = O, NH, (CH2)qO, CH2NH, OCH2, CH:CH, S, etc.; Y = CH2, C:O, C:S, C:NH, C:NMe; B = CH2(substituted) N-containing heterocyclic or heterobicyclic ring; W = CH2, C:O, CO2, SO2, C(:NCH2Ph), etc.; R1 = (hetero)aryl, C1-5 alkoxy, camphor-10-yl] are useful as oxytocin and vasopressin receptor antagonists, e.g in treatment of preterm labor and dysmenorrhea and in stopping labor preparatory to cesarean delivery. Thus, in competitive radioligand binding assays on rat uterus membrane prepns., high-affinity binding of oxytocin-3H was inhibited by 1-[1-[4-[1-[(diethylaminoethyl)sulfonyl]-4piperidinyloxy]-2-methoxybenzoyl]piperidin-4-yl]-1,2-dihydro-4H-3,1benzoxazin-2-one (II) with an IC50 of 23 nM. II was prepared in 7 steps from Me 2,4-dihydroxybenzoate, N-tert-butyloxy-4-piperidinol, 1-(4-piperidinyl)-1,2-dihydro-4H-3,1-benzoxazin-2-one-HCl (preparation given), ClCH2CH2SO2Cl, and HNEt2. Preparation of 277 compds. of formula I is described.

IT 162043-19-8P 162043-21-2P 162044-10-2P 162044-11-3P 162044-15-7P 162044-17-9P

162044-18-0P 162044-19-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(benzoxazinone and benzopyrimidinone piperidinyl tocolytic oxytocin receptor antagonists)

RN

162043-19-8 HCAPLUS
Piperidine, 1-[2-methoxy-4-[[1-[[1-(phenylmethyl)-3-pyrrolidinyl]sulfonyl]-CN 4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)- (9CI) (CA INDEX NAME)

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162043-21-2 HCAPLUS RN

CN

Piperidine, 1-[4-[[1-[(1-ethyl-3-pyrrolidinyl)sulfonyl]-4-piperidinyl]oxy]-2-methoxybenzoy1]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

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PAGE 2-A

● HCl

monohydrochloride (9CI) (CA INDEX NAME)

PAGE 2-A

HCl

RN

162044-11-3 HCAPLUS
Piperidine, 1-[2-methoxy-4-[[1-[[1-[(2-methyl-3-pyridinyl)methyl]-3-pyrrolidinyl]sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, dihydrochloride (9CI) (CA INDEX NAME) CN

PAGE 2-A

●2 HCl

RN 162044-15-7 HCAPLUS CN 1-Piperazinecarboxylic ac

1-Piperazinecarboxylic acid, 4-[[4-[3-methoxy-4-[[4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-1-piperidinyl]carbonyl]phenoxy]-1-piperidinyl]sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 2-A

162044-17-9 HCAPLUS
Piperidine, 1-[2-methoxy-4-[[1-[[4-[(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, dihydrochloride (9CI) (CA INDEX NAME) RNCN

PAGE 2-A

●2 HCl

RN 162044-18-0 HCAPLUS
CN Piperidine, 1-[2-methoxy-4-[[1-[(4-methyl-1-piperazinyl)sulfonyl]-4-piperidinyl]oxy]benzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, hydrochloride (9CI) (CA INDEX NAME)

PAGE 2-A

•x HCl

RN 162044-19-1 HCAPLUS
CN Piperidine, 1-[4-[[1-[(4-ethyl-1-piperazinyl)sulfonyl]-4-piperidinyl]oxy]2-methoxybenzoyl]-4-(2-oxo-2H-3,1-benzoxazin-1(4H)-yl)-, hydrochloride
(9CI) (CA INDEX NAME)

PAGE 2-A

●x HCl

L37 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1992:591648 HCAPLUS

DOCUMENT NUMBER:

117:191648

TITLE:

Orally active, nonpeptide oxytocin antagonists

AUTHOR(S): Evans, Ben E.; Leighton, James L.; Rittle, Kenneth E.; Gilbert, Kevin F.; Lundell, George F.; Gould, Norman

P.; Hobbs, Doug W.; DiPardo, Robert M.;

Veber, Daniel F.; et al.

CORPORATE SOURCE:

Dep. Med. Chem., Merck Res. Lab., West Point, PA,

19486, USA

SOURCE:

Journal of Medicinal Chemistry (1992), 35(21), 3919-27

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE:

LANGUAGE:

Journal English

GΙ

AB Spiroindenepiperidines, including I, were prepared as orally bioavailable oxytocin antagonists; I showed good in vivo duration. The potential use of these agents for treatment of preterm labor and their significance as new nonpeptide ligands for peptide receptors are discussed.

IT 95941-26-7P 143632-57-9P 143632-58-0P

143632-60-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and oxytocin antagonist activity of)

RN 95941-26-7 HCAPLUS

CN 4-Piperidinecarboxylic acid, 3-methyl-1-[(4-methylphenyl)sulfonyl]-4-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 143632-57-9 HCAPLUS

CN Piperidine, 1-[(4-methylphenyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)

RN 143632-58-0 HCAPLUS

CN Piperidine, 1-[(4-methylphenyl)sulfonyl]-4,4-diphenyl- (9CI) (CA INDEX NAME)

RN 143632-60-4 HCAPLUS

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=> d stat que 140 nos
L4
                STR
L10
                STR
L12
          25437 SEA FILE=REGISTRY SSS FUL L4 AND L10
L13
              5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13
L15
L16
              3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15
L17
          25432 SEA FILE=REGISTRY ABB=ON
                                          PLU=ON
                                                  L12 NOT L15
            183 SEA FILE=REGISTRY ABB=ON
L18
                                          PLU=ON
                                                  SECRETASE
           3443 SEA FILE=HCAPLUS ABB=ON
L19
                                         PLU=ON
                                                 L17
                                                  L18 OR ?SECRETASE?
L20
           2011 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                  L19 AND L20
L21
              9 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
L22
              6 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  L21 NOT L16
                                                  L19(L) INHIBIT?
L23
            450 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
L24
            372 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  L23 AND PD=<DECEMBER 8, 2003
            301 SEA FILE=HCAPLUS ABB=ON
L25
                                          PLU=ON
                                                  L24 AND PATENT/DT
L29
             78 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  L23 AND ENZYME(L) INHIBIT?
L31
             35 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  L29 AND L25
L32
             35 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  L31 NOT (L16 OR L22)
L34
             40 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                  ("JOSIEN H"/AU OR "JOSIEN H
                B"/AU OR "JOSIEN HUBERT"/AU OR "JOSIEN HUBERT B"/AU) NOT (L16
                OR L22 OR L32)
             27 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ASBEROM T"/AU OR "ASBEROM
L35
                THEODROS"/AU) NOT (L16 OR L22 OR L32 OR L34)
             85 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOBBS D"/AU OR "HOBBS D
L36
                W"/AU OR ("HOBBS DOUG W"/AU OR "HOBBS DOUGLAS"/AU) OR ("HOBBS
                DOUGLAS W"/AU OR "HOBBS DOUGLAS WALSH"/AU)) NOT (L16 OR L22 OR
                L32 OR L34 OR L35)
L37
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L38
            100 SEA FILE=HCAPLUS ABB=ON PLU=ON
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                ("SMITH ELIZABETH M"/AU OR "SMITH ELIZABETH MARGERY"/AU OR
                "SMITH ELIZABETH MELVA"/AU)
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95 SEA FILE=HCAPLUS ABB=ON PLU=ON L38 NOT (L16 OR L22 OR L32 OR
L39
                         L34 OR L35 OR L37)
                       O SEA FILE=HCAPLUS ABB=ON PLU=ON L39 AND L19
L40
=> d stat que 142 nos
                          STR
T.4
L10
                          STR
                25437 SEA FILE=REGISTRY SSS FUL L4 AND L10
L12
                        STR
L13
L15
                       5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13
                       3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15
L16
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183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE
L17
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3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17
2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?
9 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20
6 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16
450 SEA FILE=HCAPLUS ABB=ON PLU=ON L19(L)INHIBIT?
372 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND PD=<DECEMBER 8, 2003
301 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND PATENT/DT
78 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND ENZYME(L)INHIBIT?
35 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L25
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L18
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L29
L31
L32
L34
                           B"/AU OR "JOSIEN HUBERT"/AU OR "JOSIEN HUBERT B"/AU) NOT (L16
                           OR L22 OR L32)
                     27 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ASBEROM T"/AU OR "ASBEROM
L35
                           THEODROS"/AU) NOT (L16 OR L22 OR L32 OR L34)
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L36
                           W"/AU OR ("HOBBS DOUG W"/AU OR "HOBBS DOUGLAS"/AU) OR ("HOBBS
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L39
                          L34 OR L35 OR L37)
                    141 SEA FILE=HCAPLUS ABB=ON PLU=ON "GUO TAO"/AU
0 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 AND L41
L41
L42
=> d stat que 143 nos
                           STR
L4
L10
                           STR
               25437 SEA FILE=REGISTRY SSS FUL L4 AND L10
L12
L13
                           STR
L15
                        5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13
                       3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15
L16
                25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15
183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE
L17
L18
                 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE

3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17

2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?

9 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20
6 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16
450 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 (L) INHIBIT?

372 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND PD=<DECEMBER 8, 2003

301 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND PATENT/DT
78 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND ENZYME (L) INHIBIT?
L19
L20
L21
L22
L23
L24
L25
L29
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L31	35	SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L25							
L32	35	SEA FILE=HCAPLUS ABB=ON PLU=ON L31 NOT (L16 OR L22)							
L34	40	SEA FILE=HCAPLUS ABB=ON PLU=ON ("JOSIEN H"/AU OR "JOSIEN H							
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		OR L22 OR L32)							
L35	27	SEA FILE=HCAPLUS ABB=ON PLU=ON ("ASBEROM T"/AU OR "ASBEROM							
		THEODROS"/AU) NOT (L16 OR L22 OR L32 OR L34)							
L36	85	SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOBBS D"/AU OR "HOBBS D							
		W"/AU OR ("HOBBS DOUG W"/AU OR "HOBBS DOUGLAS"/AU) OR ("HOBBS							
		DOUGLAS W"/AU OR "HOBBS DOUGLAS WALSH"/AU)) NOT (L16 OR L22 OR							
		L32 OR L34 OR L35)							
L37	7	SEA FILE=HCAPLUS ABB=ON PLU=ON L36 AND L19 ·							
L38	100	SEA FILE=HCAPLUS ABB=ON PLU=ON "SMITH ELIZABETH"/AU OR							
		("SMITH ELIZABETH M"/AU OR "SMITH ELIZABETH MARGERY"/AU OR							
		"SMITH ELIZABETH MELVA"/AU)							
L39	95	SEA FILE=HCAPLUS ABB=ON PLU=ON L38 NOT (L16 OR L22 OR L32 OR							
		L34 OR L35 OR L37)							
L41	141	SEA FILE=HCAPLUS ABB=ON PLU=ON "GUO TAO"/AU.							
L43	38	SEA FILE=HCAPLUS ABB=ON PLU=ON (L39 OR L41) AND SCHERIN?/CS							
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=>									
=>		·							
=> d ib:	=> d ibib abs 143 1-38								
T 4 2 3 3 3 7 C	16. TO TOTAL	3 A MARRING CODYDIANT CASE NO CONT							

L43 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2005:346733 HCAPLUS

TITLE:

Preparation of 1-(arylsulfonyl)piperidines as

 γ -secretase inhibitors for treatment of

neurodegenerative diseases

INVENTOR(S):

Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith, Elizabeth M.; Clader, John W.; Asberom, Theodros;

Guo, Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S):

Schering-Plough Corp., USA; Pharmacopeia,

Inc.

SOURCE:

U.S. Pat. Appl. Publ., 170 pp., Cont.-in-part of U.S.

Ser. No. 663,042.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005085506	A1	20050421	US 2004-941440	20040915
US 2004048848	A1	20040311	US 2003-358898	20030205
US 2004171614	A1	20040902	US 2003-663042	20030916
PRIORITY APPLN. INFO.:			US 2002-355618P P	20020206
			US 2003-358898 A	2 20030205
			US 2003-663042 A	2 20030916

GI

Title compds. I [wherein R1 = (un) substituted (hetero) aryl; R2 = alkyl, AB XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un) substituted (hetero) aryl, etc.; R3 = H, alkyl, OH, alkoxy, etc.; R3a, R3b = independently H or alkyl; R11 = (un) substituted (hetero) aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un) substituted amino, hydrazino, (hetero) aryl, alkyl, (hetero) cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as γ-secretase inhibitors, which inhibit the deposition of β -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K2CO3. The aldehyde was converted to the alc. with NaBH4 and protected with t-BuPh2SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchlorocarbonate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited γ-secretase activity in transfected human APP cells with an IC50 value in the range of about $0.0002~\mu\text{M}$ to about 15 μM . Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

II

L43 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:158632 HCAPLUS

DOCUMENT NUMBER: 142:261556

TITLE: Preparation of aminohydroxyalkyl cyclic amine BACE-1

inhibitors having a benzamide substituent

INVENTOR(S): Cumming, Jared N.; Iserloh, Ulrich; Stamford, Andrew; Strickland, Corey; Voigt, Johannes H.; Wu, Yusheng;

Huang, Ying; Xia, Yan; Chackalamannil, Samuel;

Guo, Tao; Hobbs, Douglas W.; Le, Thuy X. H.;

Lowrie, Jeffrey F.; Saionz, Kurt W.; Babu, Suresh D.

Schering Corporation, USA; Pharmacopeia Drug PATENT ASSIGNEE(S):

Discovery, Inc

PCT Int. Appl., 118 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

GI

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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APPLICATION NO.
                                                                                         DATE
      PATENT NO.
                                 KIND
                                          DATE
                                          -----
                                                          -----
      ______
                                 _ _ _ _
                                                        WO 2004-US25018
                                          20050224
                                                                                         20040804
      WO 2005016876
                                  A2
           W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
                 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
                 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
                 LI, CH, CH, RE, LS, FW, FL, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                                           US 2003-493987P
                                                                                 P 20030808
OTHER SOURCE(S):
                                 MARPAT 142:261556
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Title compds. [I; R1 = Q1, Q2, etc.; Q3 = (CR10R11)l; Q4 = (CR12R13)n; R = CONR27R28, PO(OR29)2; R2 = H, (substituted) alkyl, cycloalkyl, AB heterocycloalkyl, cycloalkylalkyl, aryl, heteroaryl, etc.; R3, R4 = H, (substituted) alkyl; R5 = H, (substituted) alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl; R14 = 1-4 of H, (substituted) alkyl, alkenyl, alkynyl, halo, cyano, haloalkyl, cycloalkyl, aryl, heteroaryl, etc.; R27, R28 = alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, alkoxyalkyl, etc.; NR27R28 = (substituted) 3-7 membered ring; R29 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, alkoxyalkyl, etc.; l, n = 0-3; m = 0, 1; R6-R11 = H, (substituted) alkyl, cycloalkyl, aryl, heteroaryl, aralkyl, alkenyl, alkynyl, halo, NO2, cyano, etc.; R12, R13 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocycloalkyl, alkenyl, alkynyl, etc.; with provisos], were prepared Thus, title compound (II) (preparation outlined) inhibited a soluble human BACE-1

with IC50 = 1.4 nM.

L43 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:141026 HCAPLUS

DOCUMENT NUMBER: 142:240330

Preparation of cyclic amine BACE-1 inhibitors having a TITLE:

heterocyclic substituent

Cumming, Jared N.; Huang, Ying; Li, Guoqing; Iserloh, INVENTOR(S):

Ulrich; Stamford, Andrew; Strickland, Corey; Voigt,

Johannes H.; Wu, Yusheng; Pan, Jianping; Guo, Tao; Hobbs, Douglas W.; Le, Thuy X. H.; Lowrie,

Jeffrey F.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug

Discovery, Inc.

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	PATENT NO.				KIND DATE			APPLICATION NO.						DATE			
						-								-			
WO	2005	01454	40		A 1		2005	0217		WO 2	004-1	US25'	748		2	0040	804
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	NI,
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
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	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
		ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
		SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,
		SN,	TD,	TG													
US	2005	0432	90 -		A1		2005	0224	,	US 2	004-	9110	30		2	0040	804
PRIORITY APPLN. INFO.:			.:						US 2	003-4	4936	46P]	P 2	0030	808	
OTHER S	OURCE	(S):			MAR	PAT	142:	2403	30								

Ι

Disclosed are novel compds., e.g., I [R1 = azcycloalkylcarbamoyl, carbamoyl (from piperazine, piperidine or pyrrolidine derivs.); X = 0, C(R14)2, N(R); Z is -C(R14)2- or -N(R)-; t is 0, 1, 2 or 3; R, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, heterocycloalkylalkyl, alkenyl or alkynyl; R3, R4 = H, alkyl; R5 = H, alkyl, cycloalkyl, aryl, heteroaryl; R14 = H, alkyl, alkenyl, alkynyl, halo, -CN, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, heterocycloalkylalkyl, -OR35, N(R24)(R25)or SR35; R41 is alkyl, cycloalkyl, -S02(alkyl), -C(0)-alkyl, -C(0)-cycloalkyl or -alkyl-NH-C(O)CH3; W = (CR10R11)1; V = (CR12R13)n; Y1 = (Y)m; Y = CR30R31; 1 = 0 - 3; m = 0, 1; n = 0 - 3 (whereby the sum of 1 + n = 0 - 3); etc.] or a pharmaceutically acceptable salt or solvate thereof. Also disclosed are pharmaceutical compns. comprising the compds. I and methods of treating cognitive or neurodegenerative diseases with compds. I (no data). Also disclosed are pharmaceutical compns. and methods of treatment comprising compds. I in combination with other agents useful in treating cognitive or neurodegenerative diseases (no data).

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:722916 HCAPLUS

DOCUMENT NUMBER:

141:207066

TITLE:

Preparation of 1-(arylsulfonyl)piperidines as

γ-secretase inhibitors for treatment of

neurodegenerative diseases

INVENTOR(S):

Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith, Elizabeth M.; Clader, John W.; Asberom, Theodros;

Guo, Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S):

Schering-Plough Corporation, USA;

Pharmacopeia, Inc.

SOURCE:

U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S.

Ser. No. 358,898.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT	NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004 US 2004	171614	A1 A1		US 2003-663042 US 2003-358898	
	048848			WO 2004-US30191	
W:	AE, AG, A CN, CO, C GE, GH, G LK, LR, L NO, NZ, O	L, AM, AT R, CU, CZ M, HR, HU S, LT, LU M, PG, PH	T, AU, AZ, Z, DE, DK, J, ID, IL, J, LV, MA, H, PL, PT,	BA, BB, BG, BR, BW, DM, DZ, EC, EE, EG, IN, IS, JP, KE, KG, MD, MG, MK, MN, MW, RO, RU, SC, SD, SE, UG, US, UZ, VC, VN,	BY, BZ, CA, CH, ES, FI, GB, GD, KP, KR, KZ, LC, MX, MZ, NA, NI, SG, SK, SL, SY,
RW:	BW, GH, G AZ, BY, K EE, ES, F	M, KE, LS G, KZ, MI I, FR, GE R, BF, BJ	G, MW, MZ, D, RU, TJ, B, GR, HU,	NA, SD, SL, SZ, TZ, TM, AT, BE, BG, CH, IE, IT, LU, MC, NL, CI, CM, GA, GN, GQ,	UG, ZM, ZW, AM, CY, CZ, DE, DK, PL, PT, RO, SE,
US 2009 PRIORITY API	PLN. INFO.:	A1	20050421	US 2004-941440 US 2002-355618P US 2003-358898 US 2003-663042	20040915 P 20020206 A2 20030205 A 20030916

OTHER SOURCE(S):

MARPAT 141:207066

GI

Title compds. I [wherein R1 = (un) substituted (hetero) aryl; R2 = alkyl, AB XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un) substituted (hetero) aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; p = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as γ -secretase inhibitors, which inhibit the deposition of β -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K2CO3. The aldehyde was converted to the alc. with NaBH4 and protected with t-BuPh2SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited γ -secretase activity in transfected human APP cells with an IC50 value in the range of about 0.0002 μM to about 15 μM . Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

L43 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:633663 HCAPLUS

DOCUMENT NUMBER: 139:179979

TITLE: Preparation of 1-(arylsulfonyl)piperidines as

II

γ-secretase inhibitors for treatment of

neurodegenerative diseases

INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,

Elizabeth M.; Clader, John W.; Asberom, Theodros;

Guo, Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia,

Inc.

SOURCE:

PCT Int. Appl., 170 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.		APPLICATION NO.				
WO 2003066592	A1 20030814	WO 2003-US3471	20030205			
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY,	BZ, CA, CH, CN,			
CO, CR, CZ,	DE, DK, DM, DZ,	EC, EE, ES, FI, GB,	GD, GE, HR, HU,			
ID, IL, IN,	IS, JP, KG, KR,	KZ, LC, LK, LR, LT,	LU, LV, MA, MD,			
MG, MK, MN,	MX, MZ, NO, NZ,	PH, PL, PT, RO, RU,	SC, SE, SG, SK,			
		UA, UZ, VC, VN, YU,				
RW: GH, GM, KE,	LS, MW, MZ, SD,	SL, SZ, TZ, UG, ZM,	ZW, AM, AZ, BY,			
		BE, BG, CH, CY, CZ,				
FI, FR, GB,	GR, HU, IE, IT,	LU, MC, NL, PT, SE,	SI, SK, TR, BF,			
BJ, CF, CG,	CI, CM, GA, GN,	GQ, GW, ML, MR, NE,	SN, TD, TG			
CA 2478423	AA 20030814	CA 2003-2478423	20030205			
		EP 2003-737650				
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,			
		CY, AL, TR, BG, CZ,				
BR 2003007492	A 20041123	BR 2003-7492	20030205			
PRIORITY APPLN. INFO.:		US 2002-355618P				
		WO 2003-US3471				
OTHER SOURCE(S):	MARPAT 139:1799	79				

$$(R^3)_2$$

$$R^{11}$$

$$(R^3)_2$$

$$(R^3)_n$$

$$(R^3)_2$$

$$(R^3)_n$$

$$(R^3)_2$$

$$(R^3)_2$$

$$(R^3)_2$$

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$$(R^3)_2$$

$$(R^3)_2$$

$$(R^3)_2$$

$$(R^3)_2$$

$$(R^3)_3$$

$$(R^3)_4$$

$$(R^3)$$

AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloclkylene-alkylene-XCOY, or (un)substitute (hetero)aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof) were prepared as γ-secretase inhibitors, which inhibit the deposition of β-amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K2CO3. The aldehyde was converted

II

to the alc. with NaBH4 and protected with t-BuPh2SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited γ -secretase activity in transfected human APP cells with an IC50 value in the range of about 0.0002 μM to about 15 μM . Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN 2001:331328 HCAPLUS ACCESSION NUMBER:

2

DOCUMENT NUMBER:

134:326766

Preparation of amino acid derivatives of aminobenzoic TITLE:

and aminobiphenylcarboxylic acids as anti-cancer

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

agents

Blood, Christine H.; Neustadt, Bernard R.; Smith, INVENTOR (S):

Elizabeth M.

Schering Corporation, USA PATENT ASSIGNEE(S):

U.S., 29 pp. CODEN: USXXAM SOURCE:

Patent DOCUMENT TYPE: English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

REFERENCE COUNT:

KIND DATE APPLICATION NO. DATE PATENT NO. --------------US 1998-82787 В1 20010508 19980521 US 6228985 PRIORITY APPLN. INFO.: US 1998-82787 19980521

MARPAT 134:326766 OTHER SOURCE(S):

Compds. Q-NH(CH2) nC6H4C6H4CO-R or Q-NH(CH2) nC6H4CO-R [n is 0 or 1; R is NH2 or NHCHR1R2, where R1, R2 = H, alkyl, aralkyl, heteroaralkyl, carboxy, carboxyalkyl, carbamoyl; Q is R3C(0) or R4CONHCHR5CO, where R5 = H, alkyl, aralkyl, heteroaralkyl, carbamoylalkyl; R3, R4 = H, alkyl, alkoxy, arylalkoxy, aralkyl, heteroaralkyl, carbamoylalkyl (substituents in the biphenylcarboxylic and benzoic acids may not be in ortho, ortho! - and ortho-positions, resp.)] or biolabile esters or pharmaceutically acceptable salts were prepared The compds. are useful for treating urokinase-type plasminogen activator (uPA) or urokinase-type plasminogen activator receptor (uPAR)-mediated disorders, e.g., tumor metastasis, tumor angiogenesis, restenosis, chronic inflammation, or corneal angiogenesis. Thus, N-[4-[4-[(3-indolylacetyl)amino]phenyl]benzoyl]-L- $\,$ phenylalanine was prepared by the solid-phase method and showed IC50 = 20 nM for binding of radioligand c-[125I-Tyr24]-ATFp.

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

2001:227347 HCAPLUS ACCESSION NUMBER:

135:55618 DOCUMENT NUMBER:

Inhibition of angiogenesis and tumor growth by TITLE:

SCH221153, a dual $\alpha v \beta 3$ and $\alpha v \beta 5$ integrin receptor antagonist

Kumar, C. Chandra; Malkowski, Michael; Yin, Zizhang; AUTHOR (S):

Tanghetti, Elena; Yaremko, Bo; Nechuta, Terry; Varner,

Judy; Liu, Ming; Smith, Elizabeth M.;

Neustadt, Bernie; Presta, Marco; Armstrong, Lydia

CORPORATE SOURCE: Department of Tumor Biology, Schering-Plough

Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Cancer Research (2001), 61(5), 2232-2238

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal LANGUAGE: English

AB New blood vessel formation is essential for tumor growth and metastatic spread. Integrins $\alpha\nu\beta3$ and $\alpha\nu\beta5$ are arginine-glycine-aspartic acid-dependent adhesion receptors that play a critical role in angiogenesis. Hence, selective dual $\alpha\nu\beta3$ and $\alpha\nu\beta5$ antagonists may represent a novel class of angiogenesis and tumor-growth inhibitors. Here, an arginine-glycine-aspartic acid-based peptidomimetic library was screened to identify $\alpha\nu\beta3$ antagonists. Selected compds. were then modified to generate potent and selective dual inhibitors of $\alpha\nu\beta3$ and $\alpha\nu\beta5$ receptors. One of these compds., SCH 221153, inhibited the binding of

receptors. One of these compds., SCH 221153, inhibited the binding of echistatin to $\alpha v\beta 3$ (IC50 = 3.2 nM) and $\alpha v\beta 5$ (IC50 =

1.7 nM) with similar potency. Its IC50 values for related $\alpha11b\beta3$ and $\alpha5\beta1$ receptors were 1294 nM and 421 nM,

resp., indicating that SCH 221153 is highly selective for $\alpha\nu\beta3$ and $\alpha\nu\beta5$ receptors. In cell-based assays, SCH 221153 inhibited the binding of echistatin to $\alpha\nu\beta3$ - and $\alpha\nu\beta5$ -

expressing 293 cells and blocked the adhesion of endothelial cells to immobilized vitronectin and fibroblast growth factor 2 (FGF2). SCH 221153, but not the inactive analog SCH 216687, was effective in inhibiting FGF2 and vascular endothelial growth factor-induced endothelial

cell proliferation in vitro with an IC50 equal to 3-10 μ M. Angiogenesis induced by FGF2 in the chick chorioallantoic membrane assay was also inhibited by SCH 221153. Finally, SCH 221153 exerted a significant inhibition on tumor growth induced by intradermal or s.c. injection of human melanoma LOX cells in severe combined immunodeficient

mice.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:195204 HCAPLUS

DOCUMENT NUMBER: 134:237826

TITLE: Preparation of benzimidazole amino acid derivatives as

vitronectin receptor antagonists

INVENTOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 49 pp.

CODEN: USXXAM DOCUMENT TYPE: Patent

LANGUAGE: Facelite English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE -----_ _ _ _ -----______ US 6204282 B1 20010320 US 1999-450235 19991129 PRIORITY APPLN. INFO.: P 19981130 US 1998-110302P

OTHER SOURCE(S): MARPAT 134:237826

GI

Т

Benzimidazole amino acid derivs. I [X = (CR5R6)n(CR7R8)pNR3(CR9R10)q(CR11R AB 12)r, which is attached at the meta or para position of the benzene ring; n, p, q, r = 0, 1; a, b, c, d represent carbon or nitrogen atom, with the proviso that no more than two of a, b, c, and d are nitrogen atoms; Y, Y' represent 1-4 optional substituents selected from alkyl, alkoxy, halo, CF3, and CO2H; R1 = H or (un) substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl, NHRA, NHCORA, NHSO2RA, NHCONHRA, or NHCO2RA (RA = H, alkyl, aryl, aralkyl, etc.); R2 = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl; R3 = heterocycloalkylalkyl, heterocyclocycloalkyl, CORD, SO2RE, CONRFRG, CONRFSO2RE, C(:S)NRFRG (RD, RE, RF and RG = H, alkyl, aryl, aralkyl, etc.); R5-R12 = H, alkyl] or their biolabile esters or pharmaceutically acceptable salts were prepared as vitronectin receptor antagonists. Thus, N3-[4-[[(benzimidazol-2-ylmethyl)amino]methyl]benzoyl]-N2-(benzyloxycarbonyl)diaminopropionic acid, prepared by the solid phase method, showed IC50 = 5.4 nM for binding to the vitronectin ανβ3 receptor.

REFERENCE COUNT:

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:384160 HCAPLUS

DOCUMENT NUMBER:

133:30958

TITLE:

Preparation of benzimidazole amino acid derivatives as

vitronectin receptor antagonists

INVENTOR(S):

Neustadt, Bernard R.; Smith, Elizabeth M.

PATENT ASSIGNEE(S):

Schering Corporation, USA

SOURCE:

PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.					KIND DATE		DATE	PE APPLICATION NO.						DATE			
WO 2000032578					A1 20000608			WO 1999-US26023						19990929			
		AE,															
							FI,										
							LR,										
		PL,	PT,	RO,	RU,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	ΤZ,	UA,	UZ,
							BY,										
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,
		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	ΒF,	ВJ,	CF,
		CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG				
CA 2353063							CA 1999-2353063					19990929					
EP 1135374				A1		20010926			EP 1999-962691					19990929			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2002531441 T2 20020924 JP 2000-585220 19991129 PRIORITY APPLN. INFO.: US 1998-201611 A 19981130 WO 1999-US26023 W 19990929

OTHER SOURCE(S): MARPAT 133:30958

$$\begin{array}{c|c}
 & Y^1 \\
 & b \\
 & A \\
 & C \\
 & d \\
 & N \\
 & N$$

AB Benzimidazole amino acid derivs. I [X = (CR5R6)n(CR7R8)pNR3(CR9R10)q(CR11R 12)r, which is attached at the meta or para position of the benzene ring; n, p, q, r = 0, 1; a, b, c, d represent carbon or nitrogen atom, with the proviso that no more than two of a, b, c, and d are nitrogen atoms; Y, Y' represent 1-4 optional substituents selected from alkyl, alkoxy, halo, CF3, and CO2H; R1 = H or (un) substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl, NHRA, NHCORA, NHSO2RA, NHCONHRA, or NHCO2RA (RA = H, alkyl, aryl, aralkyl, etc.); R2 = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heterocycloalkyl, heterocycloalkyl, heterocycloalkylalkyl; R3 = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl, CORD, CO2RD, SO2RE, CONRFGG, CONRFSO2RE, C(:S)NRFRG (RD, RE, RF and RG = H, alkyl, aryl, aralkyl, etc.); R5-12 = H, alkyl] or their biolabile esters or pharmaceutically acceptable salts were prepared as vitronectin receptor antagonists. Thus, N3-[4-[[(benzimidazol-2ylmethyl) amino] methyl] benzoyl] -N2 - (benzyloxycarbonyl) -L-2,3diaminopropionic acid, prepared by the solid phase method, showed IC50 = 5.4

Ι

nM for binding to the vitronectin $\alpha v\beta 3$ receptor. REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:630469 HCAPLUS

DOCUMENT NUMBER: 129:331038

TITLE: Construction of a family of biphenyl combinatorial

libraries: structure-activity studies utilizing

libraries of mixtures

AUTHOR (S):

Neustadt, Bernard R.; Smith, Elizabeth M.; Lindo, Neil; Nechuta, Terry; Bronnenkant, Alan; Wu,

Arthur; Armstrong, Lydia; Kumar, Chandra

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth,

NJ, 07033-0539, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1998),

8(17), 2395-2398

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GT

AB A set of biphenyl amino acid building blocks I and II (Fmoc = 9-fluorenylmethoxycarbonyl) has been synthesized. These were used to construct partially-peptidic combinatorial libraries as equimolar multi-component samples. Activity of members of this library as vitronectin receptor antagonists is described, together with SAR studies of the most active members. These studies illustrate several important features of combinatorial libraries.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1998:454023 HCAPLUS

DOCUMENT NUMBER:

129:203251

TITLE:

Combinatorial libraries based on a novel and readily

accessible "centroid" scaffold

AUTHOR (S):

Neustadt, Bernard R.; Smith, Elizabeth M.;

Nechuta, Terry; Zhang, Yongzheng

CORPORATE SOURCE:

Schering-Plough Research Institute, Kenilworth,

NJ, 07033-0539, USA

SOURCE:

Tetrahedron Letters (1998), 39(30), 5317-5320

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER:

Elsevier Science Ltd. Journal

DOCUMENT TYPE:

English

LANGUAGE:
OTHER SOURCE(S):

CASREACT 129:203251

GΙ

AB A convenient large-scale preparation of the trifunctional acid I (Fmoc = 9-fluorenylmethoxycarbonyl) has been developed. This acid serves as a useful scaffold for construction of combinatorial libraries incorporating three variable elements in a centro-sym. array.

REFERENCE COUNT:

17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1997:436013 HCAPLUS

DOCUMENT NUMBER:

127:95514

TITLE:

Potent Tetracyclic Guanine Inhibitors of PDE1 and PDE5 Cyclic Guanosine Monophosphate Phosphodiesterases with

Oral Antihypertensive Activity

AUTHOR (S):

Ahn, Ho-Sam; Bercovici, Ana; Boykow, George; Bronnenkant, Alan; Chackalamannil, Samuel; Chow, Jason; Cleven, Renee; Cook, John; Czarniecki, Michael; Domalski, Carol; Fawzi, Ahmad; Green, Michael; Guendes, Asli; Ho, Ginny; Laudicina, Malvina; Lindo, Neil; Ma, Ke; Manna, Mahua; McKittrick, Brian; Mirzai, Bita; Nechuta, Terry; Neustadt, Bernard; Puchalski, Chester; Pula, Kathryn; Silverman, Lisa; Smith, Elizabeth; Stamford, Andrew; Tedesco, Richard P.;

Tsai, Hsingan; Tulshian, Deen; Vaccaro, Henry; Watkins, Robert W.; Weng, Xiaoyu; Witkowski, Joseph

T.; Xia, Yan; Zhang, Hongtao

CORPORATE SOURCE:

Schering-Plough Research Institute, Kenilworth,

NJ, 07033, USA

SOURCE:

Journal of Medicinal Chemistry (1997), 40(14),

2196-2210

CODEN: JMCMAR; ISSN: 0022-2623

American Chemical Society

Journal

DOCUMENT TYPE:

LANGUAGE:

PUBLISHER:

GI

English

$$\begin{array}{c|c}
R^2 & O & R \\
N & N & N \\
N & N & N
\end{array}$$

Tetracyclic guanines I, IV have been shown to be potent and selective inhibitors of the cGMP-hydrolyzing enzymes PDE1 and PDE5. In general, these compds. are inactive or only weakly active as inhibitors of PDE3, which is a major isoenzyme involved in cAMP hydrolysis. Structure-activity relationships are developed at N-1, C-2, N-3, and N-5 on the core nucleus. Compound I [R = CH2Ph; R1 = CH2C6H4Ph-4; R2 = Me (II)], with an IC50 of 70 pM, is the most potent inhibitor of PDE1, while I [R = CH2Ph; R1 = C.tplbond.CPh; R2 = Me (III)], with an IC50 of 4 nM, is the most potent inhibitor of PDE5. Compds. e.g. IV [R3 = H; R4 = cyclopentylmethyl; R5 = Me; R6,R7 = bond (V)] and III are potent dual inhibitors with IC50 values below 30 nM for both PDE1 and PDE5. Compds. I (R = H; R1 = hexyl; R2 = Me; R = H: R1 = CH2Ph; R2 = Me) and V reduced blood pressure by more than 45 mm Hg when administered orally at 10 mg/kg to the spontaneously hypertensive rat (SHR).

REFERENCE COUNT:

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

20

ACCESSION NUMBER:

1995:420794 HCAPLUS

DOCUMENT NUMBER:

123:228893

TITLE:

Carboxyalkylcarbonyl amino acid endopeptidase

inhibitors

INVENTOR(S):

Neustadt, Bernard R.; Smith, Elizabeth M.;

Haslanger, Martin F.

PATENT ASSIGNEE(S):

Schering Corp., USA

SOURCE:

U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 439,765.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO).	KIND	DATE	APPLICATION NO.	DATE
US 538961	10	Α	19950214	US 1992-849036	19920421
WO 910738		A1	19910530	WO 1990-US6655	19901120
W: A	AU, BB, BG,	BR, CA	, FI, HU,	JP, KP, KR, LK, MC, M	IG, MW, NO, RO,
S	SD, SU, US				
RW: A	AT, BE, BF,	BJ, CF	CG, CH,	CM, DE, DK, ES, FR, C	BA, GB, GR, IT,
I	LU, ML, MR,	NL, SE	, SN, TD,	TG	
PRIORITY APPLN				US 1989-439765	A2 19891121
				WO 1990-US6655	W 19901120
OTHER SOURCE (S	3) •	MARPAT	123:2288	93	

OTHER SOURCE(S):

MARPAT 123:228893

GΙ

Carboxyalkylcarbonyl amino acid inhibitors of endopeptidases of the AΒ formula I or pharmaceutically acceptable salt thereof, wherein R1 is H, alkyl, arylalkyl, aryl or aryloxyalkyl; R2 is alkyl, alkenyl, alkynyl, alkoxy or alkylthio, wherein the alkyl portion is substituted with 0-3 substituents independently selected from the group consisting of hydroxy, alkoxy, alkoxyalkoxy, alkylthio, aryl, alkoxyalkylthio, arylalkoxy and arylalkylthio; R3 and R4 are independently alkyl or arylalkyl; or R3 and R4 together with the carbon to which they are attached form an optionally substituted 5-, 6- or 7-membered ring wherein said ring comprises 0 to 1 heteroatoms selected from the group consisting of sulfur and oxygen; R5 is H, alkyl, alkoxyalkyl, alkylthioalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, arylalkoxyalkyl or arylalkylthioalkyl; R6 is H, hydroxy, alkoxy, alkyl, arylalkoxy, alkoxyalkyl, alkylthioalkyl, arylalkoxyalkyl, arylalkylthioalkyl, aryl or heteroaryl; R7 is hydroxy, alkoxy, aryloxy, arylalkoxy, amino, alkylamino or dialkylamino; m is 0 or 1; and n is 0, 1, 2 or 3, use of the compds., alone or in combination with an ACE inhibitor or an ANF, in the treatment of cardiovascular disorders such as hypertension, congestive heart failure, edema and renal insufficiency, use of the compds. in the treatment of nephrotoxicity and pain conditions (no data), and pharmaceutical compns. containing said compds. are disclosed. Pharmaceutical formulations were given. Thus, e.g., N-[1-[2(R,S)-carboxy-4-phenylbutyl]cyclopentanecarbonyl]-(L)-methionine was prepared by a consecutive series of reactions involving addition of cyclopentanecarboxylic acid with t-Bu 2-(2-phenylethyl)acrylate to afford 1-(2-t-Butoxycarbonyl-4-

phenylbutyl)cyclopentanecarboxylic acid, followed by coupling with (S) -methionine Et ester hydrochloride.

L43 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1995:264514 HCAPLUS

DOCUMENT NUMBER:

122:56581

TITLE:

Preparation of peptide analogs as inhibitors of

neutral endopeptidase and angiotensin converting

INVENTOR(S):

Neustadt, Bernard R.; Smith, Elizabeth M.;

Tulshian, Deen

PATENT ASSIGNEE(S):

Schering Corp., USA

SOURCE:

PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE	
WO 9403481	A1 19940217	WO 1993-US7137	19930803	
W: AU, BB, BG,	BR, BY, CA, CZ,	FI, HU, JP, KR, KZ,	LK, MG, MN, MW,	
NO, NZ, PL,	RO, RU, SD, SK,	UA, US, VN	•	
RW: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IE, IT, LU,	MC, NL, PT, SE,	
BF, BJ, CF,	CG, CI, CM, GA,	GN, ML, MR, NE, SN,	TD, TG	
US 5298492	A 19940329	US 1992-925338	19920804	
AU 9347919	A1 19940303	AU 1993-47919	19930803	
EP 658169	A1 19950621	EP 1993-918488	19930803	
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IE, IT, LI,	LU, MC, NL, PT, SE	
JP 07509717	T2 19951026	JP 1993-505432	19930803	
PRIORITY APPLN. INFO.:		US 1992-925338	A2 19920804	
		WO 1993-US7137	W 19930803	
OTHER SOURCE(S):	MARPAT 122:5658	1		

GΙ

$$\begin{array}{c|c} & H_2N \text{ (CH2) 4} \\ & & & \\$$

Title compds. [I; Z = amino, alkylamino, dialkylamino, R9CONH, AΒ (substituted) guanidino; R1 = H, R7R8N; R2 = H, alkyl, cycloalkyl, arylalkyl, heteroarylalkyl; R3 = H, alkyl or cycloalkyl; R2R3C = 3-7

membered carbocyclic ring; R4 = H, alkyl, arylalkyl or heteroarylalkyl;
R5, R6 = OH, alkoxy, amino, arylalkoxy, alkylamino, dialkylamino; R7 =
R9CO, R10SO2; R8 = H, alkyl, arylalkyl, aryl; R7R8N = 5-7 membered ring;
R9 = alkyl, arylalkyl, aryl, heteroarylalkyl, heteroaryl, alkoxy,
arylalkoxy, amino, alkylamino, dialkylamino; R10 = alkyl, arylalkyl, aryl,
heteroarylalkyl, amino, alkylamino, dialkylamino, heteroaryl; m, n = 1-5],
were prepared Thus, title compound II (solution phase preparation given)
inhibited

ACE with IC50 = 50 nM.

L43 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:499078 HCAPLUS

DOCUMENT NUMBER: 121:99078

TITLE: Mercaptoacyl amino acid inhibitors of atriopeptidase.

1. Structure-activity relationship studies of methionine and S-alkylcysteine derivatives

AUTHOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.;

Nechuta, Terry L.; Bronnenkant, Alan A.; Haslanger, Martin F.; Watkins, Robert W.; Foster, Caroline J.;

Sybertz, Edmund J.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth,

NJ, 07033-0539, USA

SOURCE: Journal of Medicinal Chemistry (1994), 37(15), 2461-76

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal LANGUAGE: English

AB A broad series of N-(3-mercaptoacyl) amino acid derivs. was evaluated for their ability to inhibit atriopeptidase (neutral endopeptidase, EC 3.4.24.11) in vitro and in vivo. Structural parameters studied were (i) the substituent on the 2-position of the 3-mercaptopropionyl moiety, (ii) the amino acid component, (iii) the S-terminal derivative, and (i.v.) the C-terminal derivative Optimum activity was observed for derivs. of methionine and S-alkylcysteines. N-[3-Mercapto-2(S)-[(2-methylphenyl)methyl]-1-oxopropyl]-L-methionine was identified as a highly effective inhibitor of atriopeptidase meriting evaluation as a potential cardiovascular therapeutic agent.

L43 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:236168 HCAPLUS

DOCUMENT NUMBER: 116:236168

TITLE: Preparation of (mercaptoacylamino) acids for treatment

of hypertension and congestive heart failure.

INVENTOR(S): Haslanger, Martin F.; Neustadt, Bernard R.;

Smith, Elizabeth M. Schering Corp., USA

PATENT ASSIGNEE(S): Schering Corp., USA SOURCE: U.S., 22 pp. Cont.-in-part of U.S. 4,801,609.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5061710	A	19911029	US 1987-133669	19871216
US 4801609	Α	19890131	US 1987-32153	19870327
EP 254032	A2	19880127	EP 1987-108730	19870617
EP 254032	A3	19900905		
R: AT, BE, CH	, DE, ES	S, FR, GB, G	R, IT, LI, LU, NL, SE	
JP 08283153	A2	19961029	JP 1995-246555	19870619

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US 4929641
                                  19900529
                                              US 1988-192435
                                                                      19880511
     US 4929641
                                  19940830
                           B1
     WO 8905796
                                  19890629
                                              WO 1988-US4376
                          A1
                                                                      19881213
             AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO,
             SD, SU, US
         RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL,
             SE, SN, TD,
     EP 322633
                                  19890705
                           A1
                                              EP 1988-120795
                                                                      19881213
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                           В1
                                 19910522
         R: ES, GR
     AU 8928002
                           A1
                                 19890719
                                              AU 1989-28002
                                                                      19881213
     AU 615976
                           B2
                                 19911017
     EP 390839
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                                 19901010
                                              EP 1989-900561
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         R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
     JP 02503799
                           T2
                                 19901108
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     HU 54979
                           A2
                                 19910429
                                              HU 1989-380
                                                                      19881213
     HU 204781
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                                 19920228
     AT 63741
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                                 19910615
                                              AT 1988-120795
                                                                      19881213
     ES 2039578
                           Т3
                                 19931001
                                              ES 1988-120795
                                                                      19881213
     CN 1033803
                           Α
                                 19890712
                                              CN 1988-108633
                                                                      19881214
     ZA 8809373
                                              ZA 1988-9373
                           Α
                                 19900829
                                                                      19881214
     DK 9001468
                          Α
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                                              DK 1990-1468
                                                                      19900615
     NO 9002687
                                             .NO 1990-2687
                          Α
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     US 4801609
                                              US 1991-90002282
                          В1
                                 19931109
                                                                      19910214
     US 5262436
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                                 19931116
                                              US 1991-741025
                                                                      19910806
PRIORITY APPLN. INFO.:
                                              US 1987-32153
                                                                   A2 19870327
                                              EP 1987-108730
                                                                   A 19870617
                                              US 1986-876610
                                                                   Α
                                                                      19860620
                                              JP 1987-153219
                                                                   A3 19870619
                                              US 1987-133669
                                                                   A2 19871216
                                              EP 1988-120795
                                                                   A 19881213
                                              WO 1988-US4376
                                                                   Α
                                                                      19881213
OTHER SOURCE(S):
                          MARPAT 116:236168
     Q-CH2CH[(CH2)nR1]CONHCHR2COR3 [R1 = YC6H4XC6H4; YC6H4, YC6H4S, etc.; R2 =
     alkyl, (alkylsulfonyl)alkyl, (alkylsulfinyl)alkyl, etc.; R3 =
     (substituted) hydroxy, (substituted) amino, etc.; Q = H, alkanoyl, etc.; n = 0-2; X = bond, O, S, CH2; Y = H, alkyl, cycloalkyl, alkoxy, OH, F,
     etc.] and their pharmaceutically acceptable salts, useful for treatment of
     hypertension and congestive heart failure (no data), are prepared
     S-(4-Methylbenzyl)-L-cysteine Me ester hydrochloride (preparation given) was
     acylated with 3-(acetylthio)-2-benzylpropionic acid and the resulting
     diastereomeric mixture of N-[3-(acetylthio)-2-benzylpropionyl)-S-(4-
     methylbenzyl)-L-cysteine Me ester was treated with MeOH-1N NaOH at 0 to
     -5° for 6 h to give the corresponding diastereomeric mixture of
     N-(2-benzyl-3-mercaptopropionyl)-S-(4-methylbenzyl)-L-cysteine.
L43 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                          1992:174770 HCAPLUS
DOCUMENT NUMBER:
                          116:174770
TITLE:
                          Preparation of disulfide derivatives of
                          mercaptoacylamino acids as cardiovascular agents
INVENTOR (S):
                          Haslanger, Martin F.; Neustadt, Bernard R.;
                          Smith, Elizabeth M.
PATENT ASSIGNEE(S):
                          Schering Corp., USA
SOURCE:
                          PCT Int. Appl., 46 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT:
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PATENT INFORMATION:

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APPLICATION NO.
                                                                  DATE
     PATENT NO.
                        KIND DATE
                                            ______
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                                19911128 WO 1991-US3251 19910515
     WO 9117980
                          A1
         W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO,
             SD, SU, US
         RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG
                                         AU 1991-79572
ZA 1991-3685
EP 1991-911546
     AU 9179572
                          A1
                                19911210
                                                                    19910515
     ZA 9103685
                          Α
                                19920226
                                                                    19910515
                                                                    19910515
     EP 528997
                          A1
                                19930303
     EP 528997
                          B1
                                19950201
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
     JP 05502038
                  T2 19930415 JP 1991-510190
                                                                  19910515
     JP 06102648
                          B4
                                19941214
                                            ES 1991-911546
     ES 2069893
                         Т3
                                19950516
                                                                    19910515
                                                               A2 19900517
                                            US 1990-525370
PRIORITY APPLN. INFO.:
                                            WO 1991-US3251
                                                               A 19910515
                         MARPAT 116:174770
OTHER SOURCE(S):
     [SCH2CH (CH2R1) nCONHCHR2CHR4 (CH2) t (CHR9) pCOR3]2,
     [SCH2CH(CH2R7)nCONHCHR2COR3 [R1 = alkyl, cycloalkyl, aryl, heteroaryl; R2
     = H, alkyl, cycloalkyl, hydroxyalkyl, alkoxy, HS, alkylthio, aryl, heteroaryl, aralkyloxy, aralkylthio, R3 = R5O, R5R6N, R5, R6 = H, alkyl,
     hydroxyalkyl, etc., R5R6N = 5-7-membered ring; R4, R9 = (CH2)qR8, R8 = H,
     HO, alkoxy, HS, alkylthio, aryl, heteroaryl; R7 = (substituted) Ph; n = 1, 2; p, t = 0, 1; q = 0-2] useful in treatment of cardiovascular disorders
     and pain, are prepared To N-[3-mercapto-2(S)-(2-methylbenzyl)propionyl]-(S)-
     methionine Et ester (preparation given) in absolute EtOH was added iodine/EtOH
to
     qive 1,1'-[dithiobis[2(S)-(2-methylbenzyl)-1-oxo-3,1-propanediyl]]bis-(S)-
     methionine di-Et ester, which produced a drop in pressure in the DOCA salt
     model in the atrial natriuretic factor potentiation procedure.
     Pharmaceutical formulations containing the title compds. are given.
L43 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:632870 HCAPLUS
DOCUMENT NUMBER:
                         115:232870
                         Preparation of carboxyalkylcarbonyl amino acid
TITLE:
                         endopeptidase inhibitors
                         Neustadt, Bernard R.; Smith, Elizabeth M.;
INVENTOR(S):
                         Haslanger, Martin F.
PATENT ASSIGNEE(S):
                         Schering Corp., USA
                         PCT Int. Appl., 52 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                      KIND DATE
                                           APPLICATION NO.
                                                                  DATE
     PATENT NO.
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                                            _____
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                         A1 19910530 WO 1990-US6655 19901120
     WO 9107386
         W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO,
             SD, SU, US
         RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT,
             LU, ML, MR, NL, SE, SN, TD, TG
                                            CA 1990-2069112
                                19910522
                                                                    19901120
     CA 2069112
                          AA
                                19910613 AU 1991-68802
19920909 EP 1991-900076
     AU 9168802
                          A1
                                                                   19901120
                         A1
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

EP 502075

19901120

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JP 05501111
                         T2
                                          JP 1991-500851
                               19930304
                                                                 19901120
    JP 07005530
                         B4
                               19950125
                                          JP 1990-500851
                                                                 19901120
    US 5389610
                         Α
                               19950214
                                          US 1992-849036
                                                                 19920421
PRIORITY APPLN. INFO.:
                                          US 1989-439765
                                                              A2 19891121
                                          WO 1990-US6655
                                                              A 19901120
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OTHER SOURCE(S): MARPAT 115:232870

Endopeptidase-inhibiting carboxyalkylcarbonyl amino acids R10COCHR2CH2CR3R4CONH(CHR5)m(CH2)nCHR6COR7 [I; R1 = H, alkyl, aralkyl, aryloxyalkyl; R2 = (substituted) alkyl, alkenyl, alkynyl, alkoxy, alkylthio; R3, R4 = alkyl, aralkyl, or CR3R4 = (substituted or benzo-fused) 5-7 membered ring which may contain one O or S atom; R5 = alkyl, alkoxyalkyl, alkylthioalkyl, aryl, heteroaryl, etc.; R6 = OH, alkoxy, alkyl, aralkoxy, alkoxyalkyl, etc.; R7 = OH, alkoxy, aryloxy, aralkoxy, NH2, alkylamino, dialkylamino; m = 0, 1; n = 0-3], useful as cardiovascular agents (no data), analgesics (no data), and useful for the treatment of nephrotoxicity (no data), were prepared Thus, cyclopentanecarboxylic acid was treated with 2 equiv LDA followed by Ph(CH2)2CH:CHCO2CMe3 and the product was coupled with (S)-methionine Et ester hydrochloride to give N-[1-(2-tert-butoxycarbonyl-4-phenylbutyl)cyclopentanecarbonyl] - (S) -methionine Et ester. The esters groups were sequentially hydrolyzed by treatment with TFA then 1.0N NaOH to give racemic N-[1-(2-carboxy-4-phenylbutyl)cyclopentanecarbonyl]-(S)methionine. Formulations of I were prepared

L43 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:559812 HCAPLUS

DOCUMENT NUMBER: 115:159812

TITLE: Preparation of endopeptidase-inhibiting carboxyalkyl

dipeptides as analgesics and cardiovascular agents

INVENTOR(S): Haslanger, Martin F.; Neustadt, Bernard R.;

PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	rent :	NO.			KINI	D DATE	;	APP	LICAT	I NOI	. O <i>l</i>		Ι	ATE	
						-				- ·					
WO	9105	796			A1	1991	0502	WO	1990-	US564	40		1	9901	010
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		SD,	SU,	US											
	RW:	ΑT,	BE,	BF,	ВJ,	CF, CG,	CH,	CM, DE	, DK,	ES,	FR,	GΑ,	GB,	GR,	ΙT,
		LU,	ML,	MR,	NL,	SE, SN,	TD,	TG							
AU	9065	033			A1	1991	.0516	AU	1990-	65033	3		1	9901	010
EP	4958	22			A 1	1992	0729	EP	1990-	9148	12		1	9901	010
	R:	ΑT,	BE,	CH,	DE,	DK, ES,	FR,	GB, GR	, IT,	LI,	LU,	NL,	SE		
JP	0550	1247			T2	1993	0311	JP	1990-	51384	16		1	9901	010
PRIORITY	Y APP	LN.	INFO	.:				US	1989-	42104	11	1	A2 1	9891	013
								WO	1990-	US564	10	7	A 1	9901	010

OTHER SOURCE(S): MARPAT 115:159812

GI

Endopeptidase-inhibiting carboxyalkyl dipeptides AB R1OCOCHR2NHCR3R4CONH(CHR5)m(CH2)nCHR6COR7 [R1 = H, alkyl, aralkyl aryl; R2 = H, (substituted) alkyl, alkenyl, alkynyl; R3, R4 = alkyl, aralkyl or R3R4 = (substituted) 5-7 membered ring which may contain one S or O atom; R5 = H, alkyl, alkoxyalkyl, aryl, heteroaryl, etc.; R6 = H, OH, alkoxy, alkyl, alkoxyalkyl, etc.; R7 = OH, alkoxy, aryloxy, aralkoxy, (di)alkylamino; m = 0, 1; n = 0-3] useful as analgesics (no data) and cardiovascular agents (no data), were prepared Thus, 2(R)-Acetoxy-4phenylbutyric acid (preparation given) was hydrolyzed by NaOH and the resulting hydroxy acid was converted to its benzyl ester and the latter converted to the triflate. Treatment of the triflate with tert-Bu 1-aminocyclopentane-1-carboxylate (preparation given) gave 1-[1S-benzyloxycarboxy-3phenylpropyl]aminocyclopentanecarboxylic acid as the HCl salt, which was coupled with (S)-isoserine benzyl ester. HCl to give title dipeptide I. The title dipeptides are formulated as tablets and capsules.

L43 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

1991:186065 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 114:186065

Preparation of N-(mercaptoacyl)amino acids as TITLE:

cardiovascular agents

Smith, Elizabeth M.; DeCapite, Philip M.; INVENTOR (S):

> Neustadt, Bernard R. Schering Corp., USA Eur. Pat. Appl., 30 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT ASSIGNEE(S):

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 393441	A1 19901024	EP 1990-106655	19900406
	B1 19930526		
R: GR			
ZA 9002661	A 19910130	ZA 1990-2661	19900405
CA 2051652 ·	AA 19901011	CA 1990-2051652	19900406
WO 9012003	A1 19901018	WO 1990-US1787	19900406
W: AU, BB, BG,	BR, CA, FI, HU,	JP, KP, KR, LK, MC, MG,	MW, NO, RO,
SD, SU, US			
RW: AT, BE, BF,	BJ, CF, CG, CH,	CM, DE, DK, ES, FR, GA,	GB, IT, LU,
ML, MR, NL,	SE, SN, TD, TG		
AU 9054363	A1 19901105	AU 1990-54363	19900406
AU 633079	B2 19930121		
EP 467957	A1 19920129	EP 1990-906554	19900406
R: AT, BE, CH,	DE, DK, ES, FR,	GB, IT, LI, LU, NL, SE	•
HU 58286	A2 19920228	HU 1990-3561	19900406
HU 209778	B 19941028		

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JP 04504130
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    JP 07000593
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    AT 89817
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                             19930615
                                        AT 1990-106655
                                                              19900406
                       Т3
    ES 2055207
                             19940816
                                         ES 1990-106655
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    US 5219886
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                             19930615
                                         US 1991-768647
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    NO 9103956
                             19911009
                                         NO 1991-3956
                                                              19911009
PRIORITY APPLN. INFO.:
                                         US 1989-335264
                                                          A 19890410
                                         EP 1990-106655
                                                          A 19900406
                                         WO 1990-US1787
                                                          A 19900406
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OTHER SOURCE(S): MARPAT 114:186065

AB QSCH2CH[(CH2)nR1]CONHCHR2CHR4(CH2)t(CHR5)pCOR3 [I; Q = H, CHO, alkanoyl, aroyl; R1 = (cyclo)alkyl, (hetero)aryl; R2 = H, (cyclo)alkyl, (substituted) alkyl, (hetero)aryl; R3 = (substituted) OH or NH2; R4, R5 = (CH2)qR6; R6 = H, OH, alkoxy, SH, alkylthio, heteroaryl; q = 0, 1, 2; t = 0, 1], which also inhibit enkephalinase A and thus elicit analgesic effect (no data), and a pharmaceutical composition for treating hypertension, congestive heart failure, edema, renal insufficiency, or pain (no data) containing I alone or in combination with an atrial natriuretic factor or an angiotensin converting enzyme inhibitor are prepared Thus, a mixture of 2(S)-acetylthimethyl-3-(2-methylphenyl)propionic acid, (S)-isoserine Et ester-HCl (preparation given, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide-HCl, and 1-hydroxybenzotriazole in DMF was stirred 20 h to give N-[2(S)-acetylthiomethyl-3-(2-methylphenyl)propanoyl]-(S)-isoserine Et ester. Tablets containing N-[2(S)-mercaptomethyl-3-(2-methylphenyl)propanoyl]-(S)-isoserine are prepared

L43 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:158967 HCAPLUS

DOCUMENT NUMBER: 112:158967

TITLE: Preparation of mercapto-acylamino acid

antihypertensives

INVENTOR(S):
Haslanger, Martin F.; Neustadt, Bernard Ray;

Smith, Elizabeth Melva Schering Corp., USA Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT ASSIGNEE(S):

SOURCE:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 322633	A1	19890705	EP 1988-120795	19881213
EP 322633	B1	19910522		
R: ES, GR				
US 5061710	Α	19911029	US 1987-133669	19871216
AT 63741	E	19910615	AT 1988-120795	19881213
PRIORITY APPLN. INFO.:			US 1987-133669 A	19871216
			US 1987-32153 A2	19870327
			EP 1987-108730 A	19870617
			EP 1988-120795 A	19881213

AB QSCH2CH[(CH2)nR1]CONHCHR2COR3 [I; R1 = YC6H4, YC6H4S, YC6H4O, naphthyl, furyl, thienyl, benzofuryl, benzothienyl, Ph2CH, etc.; R2 = R4(CH2)kSOn(CH2)q, R5O2C(CH2)q; R3 = OR7, NR7R8, NHCHR9CONR7R8, NHCHR9CO2R7, OCHR9CONR7R8; R4 = alkenyl, alkoxy, alkylthio, OH; R5 = dihydroalkyl, dialkoxyalkyl, alkoxyalkoxyalkyl, haloalkyl, etc.; R7, R8 = H, R5, alkyl, hydroxyalkyl, aminoalkyl, arylalkyl, etc.; R7R8N = (substituted) heterocyclyl; R9 = H, alkyl, carboxyalkyl, guanidinoalkyl, indolylalkyl, mercaptoalkyl, etc.; R10 = alkyl, hydroxyalkyl, alkoxyalkyl,

diaminoalkyl, naphthyl, furyl, thienyl, pyridyl, etc.; Q = H, R10CO; YY1 = H, alkyl, cycloalkyl, alkoxy, OH, F, Cl, Br, cyano, CH2NH2, CO2H, Ph, etc.; k = 1-3; m,n = 0-2; q = 1-4], useful as antihypertensives and adjuvants for atrial natriuretic factors or angiotencin converting enzyme inhibitors, were prepared Thus, a mixture of 3-benzoylthio-2(S)-benzylpropionic acid, S-allyl-(R)-cysteinamide hydrochloride, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1-hydroxybenzotriazole, and N-methylmorpholine was stirred 20 h in DMF to give N-[3-benzoylthio-2(S)-benzylpropionyl]-S-allyl-(R)-cysteinamide.

L43 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1989:595414 HCAPLUS

DOCUMENT NUMBER:

111:195414

TITLE:

Preparation of N-(carboxyalkyl)dipeptides for

treatment of hypertension and congestive heart failure

and pharmaceutical compositions containing them Gold, Elijah H.; Neustadt, Bernard R.; Smith,

INVENTOR(S):

Elizabeth M.

PATENT ASSIGNEE(S):

Schering Corp., USA

U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 29,293.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT: 6

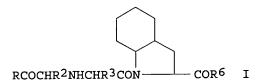
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4818749	A	19890404	US 1987-117008	19871104
EP 50800	A1	19820505	EP 1981-108348	19811015
EP 50800	B1	19860618		
EP 50800	B2	19950607		
R: AT, BE, CH,	DE, FR	R, GB, IT, LU	J, NL, SE	
ZA 8107261	Α	19820929	ZA 1981-7261	19811020
US 4808573	Α	19890228	US 1987-29293	19870323
PRIORITY APPLN. INFO.:			US 1980-199886	A2 19801023
			US 1980-201649	A2 19801028
			US 1981-258484	A2 19810428
			EP 1981-108348	A 19811015
			US 1981-334053	A2 19811223
			US 1987-29293	A2 19870323

OTHER SOURCE(S):

MARPAT 111:195414

GI



AB Angiotensin converting enzyme inhibitors I [R, R6 = OH, alkoxy; R2 = PhCH2S, PhCH2CH2SCH2, naphthylmethylthiomethyl, etc.; R3 = H, (amino)alkyl], useful for treatment of hypertension and congestive heart failure, are prepared (S)-(4-Methylbenzyl)-L-cysteine Et ester was reacted with N-pyruvoyl-(S)-perhydroindole in THF-EtOH containing NaBH3CN to give 1-[N-[1(R)-(ethoxycarbonyl)-2-(4-methylbenzylthio]ethyl]-(R,S)-alanyl]-

cis, syn-perhydroindole-2(S)-carboxylic acid. Most of the 11 I tested as inhibitors of angiotensin converting enzyme showed activity comparable to that of captopril. A total of 13 I were prepared with data. A hard gelatin capsule was formulated containing I (unspecified) 125.0, lactose 173.0, corn starch 75.0, and Mg stearate 2.0 mg is described.

L43 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:554371 HCAPLUS

DOCUMENT NUMBER: 111:154371

TITLE: Angiotensin converting enzyme inhibitors: spirapril

and related compounds

AUTHOR(S): Smith, Elizabeth M.; Swiss, Gerald F.;

Neustadt, Bernard R.; McNamara, Paul; Gold, Elijah H.;

Sybertz, Edmund J.; Baum, Thomas

CORPORATE SOURCE: Dep. Med. Chem., Schering-Plough Corp.,

Ι

Bloomfield, NJ, 07003, USA

SOURCE: Journal of Medicinal Chemistry (1989), 32(7), 1600-6

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 111:154371

GI

The synthesis of spirapril (I, R = Et, R1 = Me) (II), spiraprilat (I, R = H, R1 = Me) (III), their (RSS) stereoisomers, and their glycyl (I, R = Et, R1 = H) and lysyl [I, R = H, Et, R1 = (CH2)4NH2] analogs is described. These compds. were evaluated in vivo for inhibition of angiotensin converting enzyme (ACE), and selected compds. were evaluated for in vitro ACE inhibition (II ID50 16 μ g/kg; III IC50 0.8 nM, ID50 8 μ g/kg). In anesthetized rats (i.v.), esters II and I [R = Et, R1 = (CH2)4NH2] are more potent than enalapril, and diacids III and I [R = H, R1 = (CH2)4NH2] are more potent than enalaprilat in vitro. In the conscious rats (orally), II and enalapril showed potent and sustained activity at doses of 0.03-1 and 0.1-1 mg/kg, resp. From this work, II was selected for clin. evaluation as an antihypertensive agent.

L43 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:546828 HCAPLUS

DOCUMENT NUMBER: 111:146828

TITLE: Carboxyalkyl dipeptide derivatives as drugs for

glaucoma treatment

INVENTOR(S): Watkins, Robert; Doll, Ronald J.; Neustadt, Bernard

R.; Smith, Elizabeth M.; Magatti, Charles

V.; Gold, Elijah H.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: U.S., 17 pp. Cont.-in-part of U.S. Ser. No. 651,378.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

Engia

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4783444	A	19881108	US 1986-849072	19860404
US 4584285	Α	19860422	US 1984-651378	19840917
AU 8548088	A1	19870407	AU 1985-48088	19850916
AU 581929	B2	19890309		
EP 236307	A1	19870916	EP 1985-904731	19850916
EP 236307	B1	19910417		
R: AT, BE, CH,	DE, FR	R, GB, IT,	LI, LU, NL, SE	
JP 63500938	T2	19880407	JP 1985-504147	19850916
AT 62694	E	19910515	AT 1985-904731	19850916
FI 8702110	Α	19870513	FI 1987-2110	19870513
NO 8701982	Α	19870513	NO 1987-1982	19870513
US 4840772	Α	19890620	US 1988-227954	19880803
PRIORITY APPLN. INFO.:			US 1983-500494	A1 19830602
			US 1984-651378	A2 19840917
			EP 1985-904731	A 19850916
			WO 1985-US1744	A 19850916
			US 1986-849072	A3 19860404

OTHER SOURCE(S):

MARPAT 111:146828

GΙ

Z

$$(CH_2)_{m}CR^2NHCHR^3COWCOR^4$$
 $(CH_2)_{q}$
 (CH_2)

AB The carboxyalkyl dipeptides I (W = Q, Q1, Q2, Q3; n = 0, 1; m, p, q = 0, 1, 2; Y = CH2, CH2O, CH2S; Z = Q4, Q5; A = Cl, CF3; D = CH2, CH2CH2, CH2O, CH2S, CH2CONH; G = CONR7(CH2)t, SO2NR7(CH2)t; t = 0, 1; R1, R4 = OH, alkoxy, phenoxyalkoxy, phenylthioalkoxy, etc.; R2, R5, R6 = H, alkyl; R3 =

H, alkyl, aminoalkyl; R7 = H, alkyl, phenylalkyl] are prepared as drugs that reduce intraocular pressure (no biol. data). N-[1(S)-Ethoxycarbonyl-2-(4-nitrophenyl)ethyl]-(S)-alanine (preparation given) was reacted with benzyl cis,syn-octahydro-1H-indole-2(S)-carboxylate, in Et3N-containing DMF, at 0 to -5°, in the presence of 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide-HCl, to give benzyl 1-[N-[1(S)-ethoxycarbonyl-2-(4-nitrophenyl)ethyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylate, which upon hydrogenation over Pd/C in absolute EtOH gave 1-[N-[1-(S)-ethoxycarbonyl-2-(4-aminophenyl)ethyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylic acid. A topical solution comprised 1-[N-[1-(S)-ethoxycarbonyl-3-[4-(6-chloro-3,4-dihydro-1,1-dioxo-7-sulfamoyl-2H-1,2,4-benzothiadiazine)acetamidophenyl]propyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylic acid 10.0, Na2HPO4 10.4, NaH2PO4 2.4, chlorobutanol 5.0, hydroxypropylmethylcellulose 5.0 mg and water to 1 mL. The pH was adjusted to 7.4.

L43 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:497735 HCAPLUS

DOCUMENT NUMBER: 111:97735

TITLE: Preparation of proline- and perhydroindolecarboxylate-

containing dipeptides as antihypertensives

INVENTOR(S): Gold, Elijah H.; Neustadt, Bernard R.; Smith,

Elizabeth M.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: U.S., 6 pp. Cont.-in-part of U.S. Ser. No. 258,484,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4808573	A.	19890228	US 1987-29293	19870323
EP 50800	A1	19820505	EP 1981-108348	19811015
EP 50800	B1	19860618		
EP 50800	B2	19950607		
R: AT, BE, CH,	DE, FR	, GB, IT, LU	, NL, SE	
ZA 8107261	Α	19820929	ZA 1981-7261	19811020
US 4818749	Α	19890404	US 1987-117008	19871104
PRIORITY APPLN. INFO.:			US 1980-199886	A2 19801023
			US 1980-201649	A2 19801028
			US 1981-258484	A2 19810428
			EP 1981-108348	A 19811015
			US 1981-334053	A2 19811223
			US 1987-29293	A2 19870323

OTHER SOURCE(S): MARPAT 111:97735

GI

The title compds. [I and II; R1, R4 = OH, alkoxy; R2 = PhCH2SCH2, AB PhCH2CH2SCH2, naphthylmethylthiomethyl, methylbenzylthiomethyl, 2-(carboxyphenyl)ethyl, 2-(alkoxycarbonylphenyl)ethyl; R3 = H, alkyl, aminoalkyl; R5 = benzyloxyalkyl, benzylthioalkyl], useful as angiotencin converting enzyme (ACE) inhibitors (no data), were prepared A mixture of S-benzyl-L-cysteine Et ester, N-pyruvoyl-L-proline, and 5Å sieves was stirred 2 days in THF. NaBH3CN in EtOH was added and the mixture was stirred 18 h to give N-[(1R)-ethoxycarbonyl-2-benzylthioethyl]-(R,S)alanyl-(S)-proline-HCl.

L43 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:173745 HCAPLUS

DOCUMENT NUMBER: 110:173745

Carboxyalkyl dipeptides with atrial natriuretic factor TITLE:

potentiating and antihypertensive activity

Haslanger, Martin F.; Sybertz, Edmund J.; Neustadt, AUTHOR (S):

Bernard R.; Smith, Elizabeth M.; Nechuta,

Terry L.; Berger, Joel

Dep. Chem. Res., Schering-Plough Res., Bloomfield, NJ, 07003, USA CORPORATE SOURCE:

Journal of Medicinal Chemistry (1989), 32(4), 737-9 SOURCE:

CODEN: JMCMAR; ISSN: 0022-2623

Journal DOCUMENT TYPE: English LANGUAGE:

CASREACT 110:173745 OTHER SOURCE(S):

GI

$$\begin{array}{c|c} & \text{HO}_2\text{C} & \text{CH}_2\text{Ph} & \text{OH} \\ & & \text{PhCH}_2\text{CH}_2 & \text{N} & \text{H} \\ & & & \text{O} & & \text{I} \end{array}$$

Carboxyalkyl dipeptide I was prepared by solution methods. I and related AB carboxyalkyl dipeptides inhibited neutral endopeptidase (NEP), a protease which inactivates atrial natriuretic factor (ANF) in vitro. These inhibitors of NEP potentiate the hypotensive activity of exogenous ANF and express antihypertensive activity in a rodent model of volume-dependent hypertension. Although the precise role of ANF in the antihypertensive action of I remains to be established, these results suggest that inhibition of NEP represents a novel mechanism by which to reduce arterial blood pressure.

L43 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1988:448448 HCAPLUS

DOCUMENT NUMBER:

109:48448

TITLE:

Neutral metalloendopeptidase inhibitors in the treatment of hypertension, compositions and kits containing the inhibitors, manufacture of the

compositions, compounds of the compositions and their

preparation

INVENTOR(S):

Haslanger, Martin F.; Sybertz, Edmund, Jr.; Neustadt,

APPLICATION NO.

DATE

Bernard R.; Smith, Elizabeth M.

PATENT ASSIGNEE(S):

SOURCE:

Schering Corp., USA Eur. Pat. Appl., 167 pp.

CODEN: EPXXDW

DATE

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KTND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

PAI	LENI NO.			KIND	DAIE	APPLICATION NO.		DATE
EP	254032			A2	19880127	EP 1987-108730		19870617
EP	254032			A 3	19900905			•
	R: AT,	BE,	CH,	DE, E	S, FR, GB,	GR, IT, LI, LU, NL,	SE	
US	4749688			Α	19880607	US 1986-876610		19860620
US	4801609			Α	19890131	US 1987-32153		19870327
EP	566157			A1	19931020	EP 1993-107499		19870617
	R: AT,	BE,	CH,	DE, E	S, FR, GB,	GR, IT, LI, LU, NL,	SE	
FI	8702720			Α	19871221	FI 1987-2720 AU 1987-74458		19870618
AU	8774458			A1	19871224	AU 1987-74458		19870618
AU	602701				19901025			
ZA	8704413			Α	19880224	ZA 1987-4413		19870618
HU	44940			A2	19880530	HU 1987-2786		19870618
$_{ m IL}$	82908				. 19910916	IL 1987-82908		19870618
DK	8703138			Α	19871221	DK 1987-3138		19870619
NO	8702589			Α	19871221			19870619
JP	63039855			A2	19880220	JP 1987-153219		19870619
JP	2542620			B2	19961009			
	08283153				19961029			19870619
	5061710				19911029	US 1987-133669		19871216
AU	9068517				19910718	AU 1990-68517		19901227
	636423			B2	19930429			•
	4801609				19931109	US 1991-90002282		19910214
	5262436			Α				19910806
	08176100			A2	19960709	JP 1995-246554		19950821
PRIORITY	APPLN.	INFO	.:			US 1986-876610		
						US 1987-32153		19870327
						EP 1987-108730		
						JP 1987-153219		19870619
						US 1987-133669	A3	19871216
OTHER SC	OURCE(S):			MARPA'	T 109:4844	8		

OTHER SOURCE(S): MARPAT 109:48448

Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for preparation of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. S-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepared by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4methylbenzyl)-L-cysteine in MeOH, heating the mixture under reflux for 90 min, cooling to room temperature, and concentrating in vacuo. Rats with induced

hypertension were dosed s.c. with N-(N-[L-1-(2,2-dimethyl-1-oxopropoxy)methoxy]carbonyl)-2-phenylethyl)-L-phenylalanine]- β -alanine and 1-[(2S)-3-mercapto-2-methyl-1-oxypropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mMHg vs. an increase of 14, 11, 11, and 8 with the NMEP inhibitor alone and a decrease of 11, 7, 1, and 1 mMHg with the ACE inhibitor alone.

L43 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:438215 HCAPLUS

DOCUMENT NUMBER: 109:38215

TITLE: Synthesis and pharmacological activity of

angiotensin-converting enzyme inhibitors:
N-(mercaptoacyl)-4-substituted-(S)-prolines

AUTHOR(S): Smith, Elizabeth M.; Swiss, Gerald F.;

Neustadt, Bernard R.; Gold, Elijah H.; Sommer, Jane A.; Brown, Arthur D.; Chiu, Peter J. S.; Moran, Rosa;

Sybertz, Edmund J.; Baum, Thomas

CORPORATE SOURCE: Dep. Med. Chem., Schering-Plough Corp.,

Bloomfield, NJ, 07003, USA

SOURCE: Journal of Medicinal Chemistry (1988), 31(4), 875-85

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 109:38215

GΙ

$$R^{1}$$
 R^{2} R^{2

Title compds. I (R = R,S-Me, H; R1 = H, OH, OMe, SH, SMe, F, CN, etc.; R2 = H, OH, OMe, F, etc.; R1R2 = OCH2CH2O, SCH2CH2S) were prepared These compds. were evaluated in vitro for inhibition of angiotensin-converting enzyme (ACE), and selected compds. were evaluated in vivo for ACE inhibition. The most potent compds. in vitro are I [R = R,S-Me; R1R2 = OCH2CH2O, OCH2CMe2CH2O, SCH2CH2S, S(CH2)3S; R = H, R1R2 = SCH2CH2S]. The most potent compds. in vivo are I [R = R,S-Me; R1R2 = OCH2CH2O, SCH2CH2S, S(CH2)3S; R = H, R1R2 = SCH2CH2S, S(CH2)3S; R = R,S-Me, R1 = OMe, R2 = H].

L43 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:180075 HCAPLUS

DOCUMENT NUMBER: 108:180075

TITLE: Topical ocular hypotensive effects of the novel

angiotensin-converting enzyme inhibitor SCH 33861 in

conscious rabbits

AUTHOR(S): Watkins, Robert W.; Baum, Thomas; Cedeno, Karen;

Smith, Elizabeth M.; Yuen, Pui Ho; Ahn, Ho

Sam; Barnett, Allen

CORPORATE SOURCE: Dep. Pharmacol., Schering Res., Bloomfield,

NJ, USA

SOURCE: Journal of Ocular Pharmacology (1987), 3(4), 295-307

CODEN: JOPHER; ISSN: 8756-3320

DOCUMENT TYPE: Journal LANGUAGE: English

SCH 33861 is a novel, nonsulfhydryl, angiotensin converting enzyme (ACE) inhibitor. Topical administration of the compound to the eye of conscious rabbits was employed to examine actions on intraocular pressure (IOP). Falls in IOP resulted from SCH 33861 (0.001-0.01%) administration. Ocular hypotensive responses were sustained for as long as 24 h following a single application of 0.001% SCH 33861. The RSS isomer of SCH 33861, which is 200-fold weaker an ACE inhibitor than SCH 33861, caused only transient falls in IOP at 0.1% concentration The magnitude of the fall in IOP induced by 0.001% SCH 33861 (4.8 mmHg) was comparable to that produced by 0.5% timolol (4.5 mmHg). Other ACE inhibitors such as captopril (0.1%) and enalaprilic acid (0.01%) also reduced IOP by 4.0 and 4.7 mmHg, resp. These findings indicate that SCH 33861 is 500-fold more potent on a weight basis than is timolol in lowering IOP. No loss of ocular hypotensive activity was observed when SCH 33861 was administered twice daily for 5 days suggesting little, if any, potential for tolerance development. SCH 33861, as well as the other ACE inhibitors, caused neither ocular irritation nor alteration of pupil diameter These findings suggest that inhibition of ocular ACE may represent an effective means of reducing IOP.

L43 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1987:440330 HCAPLUS

DOCUMENT NUMBER:

107:40330

TITLE:

Preparation of amino acid derivatives as antihypertensive agents, and pharmaceutical

compositions containing them

INVENTOR (S):

Nevstadt, Bernard Ray; Smith, Elizabeth Melva ; Magatti, Charles Victor; Gold, Elijah Herman

PATENT ASSIGNEE(S): SOURCE:

Schering Corp., USA

S. African, 50 pp.

CODEN: SFXXAB

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 8600083	Α	19860827	ZA 1986-83	19860106
PRIORITY APPLN. INFO.:			ZA 1986-83	19860106

GT For diagram(s), see printed CA Issue. ΔR

The title compds. [I; R = substituted Ph, 2H-1,2,4-benzothiadiazin-3-yl; R1, R4 = OH, (un) substituted alkoxy; R2, R6 = H, alkyl; R3 = H, (amino) alkyl; W = Q1-Q4; Y = CH2, CH2O, CH2S; Z = (CH2)n, CH2O, CH2S, CH2CONH, CONR5 (CH2) p, SO2NR5 (CH2) p; R5 = H, (phenyl) alkyl; m = 0-2; n = 1, 2; p, z = 0, 1; x, y = 0-2; x + y = 1, 2] were prepared as angiotensin-converting enzyme inhibitors, useful as antihypertensives and in treatment of glaucoma. 4-Nitro-L-phenylalanine Et ester-HCl was N-alkylated with (R)-F3CSO3CHMeCO2CMe3 to give N-[1(S)-(ethoxycarbonyl)-2-(4-nitrophenyl)ethyl]-S-alanine tert-Bu ester. The latter was converted in 5 steps to 1-{N-[1(S)-(ethoxycarbonyl)-2-[4-(4-chloro-3sulfamoylbenzamido)phenyl]ethyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylic acid (II). In rats selected I inhibited angiotensin I-induced hypertension with ED50 of 33 μ g/kg and 36 μ g/kg, i.v. Formulations containing I are given.

L43 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 1986:626337 HCAPLUS

DOCUMENT NUMBER:

105:226337

TITLE:

cis, endo-Octahydrocyclopenta[b]pyrrole-2-carboxylate

INVENTOR(S):

Gold, Elijah Herman; Neustadt, Bernard Ray;

Smith, Elizabeth Melva

PATENT ASSIGNEE(S):

Schering Corp., USA PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT 1	. 07			KINI)	DATE			API	PLICATIO	N NO.			DATE
WO	8600		DK,	JP	A1	-	1986	0213		WO	1985-US	1406	- 		19850726
	RW:	AT,	BE,	CH,	DE,	FR	, GB,	ΙT,	LU,	NI	L, SE				
US	4587	258			Α		1986	0506		US	1984-63	5390			19840730
AU	8546	718			A1		1986	0225		ΑU	1985-46	718			19850726
AU	5819	19			B2		1989	0309							
JP	6150	2818			T2		1986	1204		JP	1985-50	3359			19850726
DK	8601	408			Α		1986	0326		DK	1986-14	08			19860326
US	4831	157			Α		1989	0516		US	1988-25	0300			19880928
PRIORITY	APP	LN.	INFO	. :						US	1984-63	5390	Α		19840730
										US	1980-19	9886	Α	2	19801023
										US	1980-20	1649	Α	2	19801028
										US	1981-25	8484	Α	2	19810428
										ΕP	1981-10	8348	Α		19811015
										WO	1985-US	1406	Α		19850726
										US	1986-81	7639	Α	3	19860110

GΙ

The title compds. I (R, R3 = OH, alkoxy, alkenoxy, aryloxy, aminoalkoxy, etc.; R1 = H, (un)substituted C1-10 alkyl, alkoxy, aryloxy, heteroaryloxy, NH2, etc.; R2 = H, alkyl, Ph, hydroxyphenyl, acylamino, etc.), useful intermediates for angiotensin-converting enzyme inhibitors, were prepared Thus, 1-[(S)-alanyl]cis-endo-octahydrocyclopenta[b]pyrrole-2(S)-carboxylic acid, prepared in 3 steps from Et cis, endo-octahydrocyclopenta[b]pyrrole-2-carboxylate, in MeOH was condensed with PhCH2CH2COCOEt to give 1-[N-(1(R,S-carbethoxy-3-phenylpropyl)-(S)-alanyl]-cis,endo-octahydrocyclopenta[b]pyrrole-2(S)-carboxylic acid.

L43 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1986:534346 HCAPLUS

DOCUMENT NUMBER:

105:134346

TITLE:

Peptides as angiotensin-converting enzyme inhibitors

INVENTOR(S):

Gold, Elijah H.; Neustadt, Bernard R.; Smith,

Elizabeth M.

PATENT ASSIGNEE(S):

Schering Corp., USA

SOURCE:

U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 258,484.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	TENT NO.			KINI		APPLICATION NO.		DATE
US	4587258					US 1984-635390		19840730
EP	50800			A1		EP 1981-108348		
EP	50800			В1				
					19950607			
	R: AT	, BE,	CH,	DE,	FR, GB, IT,	LU, NL, SE		
ZA	8107261			A	19820929	ZA 1981-7261		19811020
WO	8600896			A1	19860213	WO 1985-US1406		19850726
	W: AU	, DK,	JP					
	RW: AT	, BE,	CH,	DE,	FR, GB, IT,	LU, NL, SE		
						AU 1985-46718		19850726
					19890309			
EP	190224			A1	19860813	EP 1985-903779		19850726
						LI, LU, NL, SE		
JP	6150281	8		T 2	19861204	JP 1985-503359		19850726
ZA	8505659			Α	19870325	ZA 1985-5659		19850726
CA	1244041			A1	19881101	CA 1985-487583		19850726
DK	8601408			Α	19860326	DK 1986-1408		19860326
US	4831157			Α	19890516	US 1988-250300		19880928
PRIORITY	Y APPLN.	INFO	.:			US 1980-199886	A2	19801023
						US 1980-201649	A2	19801028
						US 1981-258484	A2	19810428
						EP 1981-108348	Α	19811015
						US 1984-635390	Α	19840730
						WO 1985-US1406	Α	19850726
						US 1986-817639	A 3	19860110
OTHER SO	OURCE(S)	:		CASE	REACT 105:13	4346		

GI

R1COCHR2NHCHR3CON-COR4 I

Proline derivative peptides I (R1 and R4 are OH, alkoxy, alkenyloxy, NH2, AB mono- or dialkylamino, etc.; R2 = H, alkyl, hydroxyalkyl, aminoalkyl, indolylalkyl, aralkyl, etc.; R3 = H, alkyl, phenylalkyl, hydroxyalkyl, aminoalkyl, etc.) were prepared, and they are useful in the treatment of glaucoma (no data). I (R1 = OEt, R2 = PhCH2CH2, R3 = Me, R4 = OH) was prepared in a series of reactions.

L43 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1986:479362 HCAPLUS

DOCUMENT NUMBER:

105:79362

TITLE:

Alanylindole antihypertensive agents

INVENTOR (S):

Doll, Ronald J.; Neustadt, Bernard R.; Smith, Elizabeth M.; Magatti, Charles V.; Gold, Elijah

Η.

PATENT ASSIGNEE(S):

Schering Corp., USA

SOURCE:

U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 500,494,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

. .

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT NO.			KINI	DA'	ΓE	API	PLICATION NO	•	DATE
	4584285							1984-651378		
WO.	8701707			Δ1	19	870326	WO	1985-US1744		19850916
	W: AU							1703 001/11		
							LU. NI	L, SE		
ΔIJ	8548088	, 22,	U 11,	A1	19	870407	AU	1985-48088		19850916
AU	581929			B2	19	890309				
EP	236307			A1	19	870916	EP	1985-904731		19850916
EP	236307			В1	19	910417				
								J, NL, SE .		
								1985-4245		19850916
HU	43620 199507			В	19	900228				
JP	6350093	8		T2	19	880407	JP	1985-504147 1985-904731		19850916
AT	62694			E	19	910515	AT	1985-904731		19850916
IL	77451			AT	19	900712	$_{ m IL}$	1985-77451		19851226
CA	1276396 4691049			A1	19	901113	CA	1986-499291		19860109
US	4691049	•		Α	19	870901		1986-831383		
	4783444							1986-849072		
						870513		1987-2110		
NO	8701982			Α	19	870513	NO	1987-1982		19870513
US	4840772			Α	19	890620		1988-227954		
PRIORITY	APPLN.	INFO	. :					1983-500494		
								1984-651378		
								1985-904731		
								1985-US1744		
							US	1986-849072	A3	19860404

OTHER SOURCE(S):

CASREACT 105:79362

GΙ

$$\mathbb{R}^1$$
 \mathbb{Z}^1 (CH₂) \mathbb{R}^2 (COR³) NHCHR⁴COZ²COR⁵

I

 \mathbb{C}^1
 \mathbb{C}^1
 \mathbb{C}^2
 \mathbb{C}^2
 \mathbb{C}^2
 \mathbb{C}^2
 \mathbb{C}^2
 \mathbb{C}^2
 \mathbb{C}^2

AB Amino acid derivs. I [R1 = benzothiadiazinylalkyl, chloro(sulfamoyl)benzamido, etc.; Z1 = CH2, CH2O, CH2S; n = 0-2; R2 = H, alkyl; R3, R5 = OH, alkoxy, etc.; R4 = H, alkyl, aminoalkyl; Z2 = proline

residue, octahydroindole analog, etc.] were prepared, and they are useful as antihypertensives (no data). Alanine derivative II was prepared from the reaction product of $4-O2NC6H4CH2CH(NH2)CO2Et\cdot HCl$ and BrCHMeCO2CMe3 in a series of reactions.

L43 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1985:96083 HCAPLUS

DOCUMENT NUMBER:

102:96083

TITLE:

7-Carboxyalkylaminoacyl-1,4-dithia-7-azaspiro[4.4]nonane-8-carboxylic acids

INVENTOR (S):

Gold, Elijah H.; Neustadt, Bernard R.; Smith,

Elizabeth M.

PATENT ASSIGNEE(S):

Schering Corp., USA

SOURCE:

U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 258,484.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	AP.	PLICATION NO.		DATE
US 4470972	Α	19840911	US	1982-446929		19821206
ZA 8107261	Α	19820929	ZA	1981-7261		19811020
US 5348944	Α	19940920	US	1988-261815		19880404
PRIORITY APPLN. INFO.:			US	1980-199886	A2	19801023
•			US	1980-201649	A2	19801028
			US	1981-258484	A2	19810428
OTHER SOURCE(S):	CASREA	CT 102 · 96083				

OTHER SOURCE

CASREACT 102:96083

GI

AB Title compds. I (R = alkyl, PhCH2, PhCH2S, PhCH2O, PhS, PhO; R1 = OH, alkoxy; R2 = H, alkyl, aminoalkyl) were prepared as antihypertensives (no sp. data). Thus, 4-oxo-L-proline II (Z = PhCH2O2C) was treated with HSCH2CH2SH in HOAc containing p-MeC6H4SO3H to give 1,4-dithia-7-azaspiro[4.4] nonane III (R3 = Z, R4 = Me), which was Z-deblocked by HBr/HOAc to give III.HBr (R3 = H, R4 = Me), which was condensed with

Z-L-Ala-ONSu (NSu = succinimido) to give III (R3 = Z-L-Ala, R4 = Me). The latter was saponified to give III (R3 = Z-L-Ala, R4 = H), which was Z-deblocked by HBr/HOAc to give III.HBr (R3 = H-L-Ala, R4 = H). The latter underwent reductive alkylation with PhCH2CH2COCO2Et in the presence of NaBH3CN to give title compound IV (R4 = Et), which was saponified to give IV (R4 = H).

L43 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:407052 HCAPLUS

DOCUMENT NUMBER: 101:7052

TITLE: Benzoquinolinones

INVENTOR(S): Smith, Elizabeth Melva; Doll, Ronald James;

Neustadt, Bernard Ray Schering Corp., USA

PATENT ASSIGNEE(S): Schering Corp., USA SOURCE: Eur. Pat. Appl., 49 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 102046	A1	19840307	EP 1983-108240		19830822
R: AT, BE, CH,	DE, FR	, GB, IT, LI	, NL, SE		
US 4511569	Α	19850416	US 1982-411764		19820826
US 4474786	Α	19841002	US 1983-505050		19830616
JP 59059665	A2	19840405	JP 1983-156220		19830826
PRIORITY APPLN. INFO.:			US 1982-411764	Α	19820826
			US 1983-505050	Α	19830616

OTHER SOURCE(S): CASREACT 101:7052
GI For diagram(s), see printed CA Issue.

Fused pyridinones I [R = H, alkyl; R1 = H, OH, alkoxy, cyano, alkyl, halo, (un) substituted amino or carbamoyl, acylamino, CO2H, esterified CO2H, CSNH2, C(:NH)NH2; Z = CH:CH, (CH2)n (n = 1-4), (CH2)pS(O)m(CH2)r or (CH2)pO(CH2)r (m = 0, 1, 2; p and r are 0-3); Z1 forms an optionally substituted fused benzo or pyrido], useful as cardiovascular agents (no data), were prepared 1-[(Dimethylamino)methylene]-2-tetralone was treated with NCCH2CONH2 and NaOMe and DMF at 80° to give I (R = H, R1 = cyano, Z = CH2CH2, Z1 = benzo).

L43 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:175294 HCAPLUS

DOCUMENT NUMBER: 100:175294

TITLE: Carboxyalkyl dipeptides and pharmaceutical

compositions containing them

INVENTOR(S): Smith, Elizabeth M.; Witkowski, Joseph T.;

Doll, Ronald J.; Gold, Elijah H.; Neustadt, Bernard

R.; Yehaskel, Albert S.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: Eur. Pat. Appl., 134 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
		-		
EP 88350	A1	19830914	EP 1983-102014	19830302

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EP 88350
                         B1
                               19850220
        R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE
     US 4431644
                        Α
                               19840214
                                          US 1982-355638
                                                                 19820308
     US 4431645
                         Α
                               19840214
                                          US 1982-355639
                                                                 19820308
     ZA 8300362
                         Α
                               19840926 ZA 1983-362
                                                                 19830119
                               19850315 AT 1983-102014
     AT 11921
                        E
                        Α
     NO 8300737
                               19830909 NO 1983-737
     AU 8312035
                        A1
                               19830915 AU 1983-12035
                                                                 19830303
     AU 557795
                        B2
                               19870108
     GB 2117777
                        A1
                               19831019
                                          GB 1983-5837
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     GB 2117777
                        B2
     ES 520261
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                                         ES 1983-520261
                                                                 19830303
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                               19830909 DK 1983-1101
                                                                 19830304
     JP 58162561
                        A2
                               19830927
                                         JP 1983-35707
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                               19830909 FI 1983-752
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                        B 19880530
     ZA 8301844
                        Α
                               19840627
                                          ZA 1983-1844
                                                                 19830316
PRIORITY APPLN. INFO.:
                                                            A 19820308
                                          US 1982-355638
                                                            A 19820308
                                          US 1982-355639
                                          US 1982-360532
                                                             A 19820322
                                          ZA 1983-362
                                                             A 19830119
                                          EP 1983-102014
                                                           A 19830302
OTHER SOURCE(S):
                        CASREACT 100:175294
     For diagram(s), see printed CA Issue.
AB
     Title compds. RCH2CR1(CO2H)-NHCH[(CH2)nXR2]CO-X1-OH [R = alkyl, PhCH2,
     PhCH2O, PhCH2S, PhO, PhS; R1 = H, alkyl; X = S, R2 = substituted
     (3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazin-3-yl 1,1-dioxide) methyl; X
     = NR3 (R3 = H, alkyl, Ph), R2 = sulfamoyl-substituted Bz, PhSO2, or
     benzyl; XR2 = sulfamoyl-substituted N-containing heterocyclic ring; n = 1-6;
     X1 = (un)substituted Pro or related N-containing heterocyclic amino acid
     residues] were prepared as antihypertensives and agents for the treatment of
     congestive heart failure and glaucoma (no data). Thus, H-L-Lys(Z)-OH(Z=
     CO2CH2Ph) was treated with PhCH2CH2COCO2Et and NaBH3CN to give
     (S)-PhCH2CH2CH(CO2Et)-L-Lys(Z)-OH, which was condensed with indole I to
     give dipeptide II (R4 = Z, R5 = CH2Ph), which was deblocked by
     hydrogenolysis to give II (R4 = R5 = H), which was sulfonylated with
     4-chloro-3-sulfamoylbenzenesulfonyl chloride to give title compound III.
L43 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                        1982:616730 HCAPLUS
DOCUMENT NUMBER:
                        97:216730
TITLE:
                        Carboxyalkyl dipeptides and pharmaceutical
                        compositions containing them
INVENTOR(S):
                        Neustadt, Bernard R.; Gold, Elijah H.; Smith,
                        Elizabeth M.
PATENT ASSIGNEE(S):
                        Schering Corp., USA
SOURCE:
                        Eur. Pat. Appl., 123 pp.
                        CODEN: EPXXDW
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 50800	A1	19820505	EP 1981-108348	19811015
EP 50800	B1	19860618		
EP 50800	B2	19950607		
R: AT, BE, CH	, DE, FR	, GB, IT, LU		

AT 20469	E	19860715	ΑT	1981-108348		19811015
DK 8104625	Α	19820424	DK	1981-4625		19811020
DK 161523	В	19910715				
DK 161523	C	19911223				
FI 8103283	Α	19820424	FI	1981-3283		19811020
FI 83222	В	19910228				
FI 83222	C	19910610				
AU 8176614	A1	19820429	AU	1981-76614		19811020
AU 554362	B2	19860821				
ZA 8107261	Α	19820929	ZA	1981-7261		19811020
NO 8103546	Α	19820426	ИО	1981-3546		19811021
NO 164983	В	19900827				
NO 164983	C	19901205				
JP 57112359	A2	19820713	JP	1981-168511		19811021
JP 01032240	B4	19890629				
ES 506414	A1	19831001	ES	1981-506414		19811021
IL 64085	A1	19861231		1981-64085		19811021
HU 32785	0	19840928	HU	1981-3078		19811022
HU 193146	В	19870828				
US 4587258	Α	19860506		1984-635390		19840730
US 4808573	Α	19890228		1987-29293		19870323
US 4818749	Α	19890404		1987-117008		19871104
US 4831157	Α	19890516		1988-250300		19880928
JP 01163197	A2	19890627		1988-283542		19881109
PRIORITY APPLN. INFO.:				1980-199886	Α	19801023
				1981-258484	Α	19810428
				1980-201649	A2	19801028
				1981-108348	Α	19811015
				1981-334053		19811223
				1984-635390		19840730
				1985-US1406	Α	19850726
				1986-817639	A3	19860110
			US	1987-29293	A2	19870323
CT						

GI

AB RCOCR1R2NHCHR3CONR4CR5R7COR6 [R, R6 = OH, (un) substituted alkoxy, alkenyloxy, (un) substituted NH2; R1 = H, (un) substituted alkyl; R2, R7 = H, (un) substituted alkyl; R3 = H, (un) substituted alkyl, (un) substituted phenylalkyl; R4, R5 = H, (un) substituted alkyl; R4R5 form ring systems] were prepared as antihypertensives and angiotensin-converting enzyme inhibitors (no data). Thus, H-L-Ala-OCH2Ph tosylate was treated with PhCH2CH2COCO2Et and reduced with NaBH3(CN) and then debenzylated by hydrogenolysis to give (S)-PhCH2CH2CH(CO2Et)-L-Ala-OH. The latter was condensed with cis,syn-octahydroindole-2(S)-carboxylic acid benzyl ester to give indole I (R8 = CH2Ph), which was debenzylated by hydrogenolysis to give I (R8 = H).

L43 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1975:73298 HCAPLUS

DOCUMENT NUMBER:

82:73298

TITLE:

Thermal and photolytic rearrangement of 4,6-unsaturated 4-azido-3-ketosteroids to 6-unsaturated 5β-cyano-A-nor-3-ketosteroids

AUTHOR (S):

Smith, Elizabeth M.; Shapiro, Elliot L.;

Teutsch, George; Weber, Lois; Herzog, Hershel L.; McPhail, Andrew T.; Tschang, Pui-Sen Wong; Meinwald,

Jerrold

CORPORATE SOURCE:

Nat. Prod. Res. Dep., Schering Corp.,

Bloomfield, NJ, USA

SOURCE:

Tetrahedron Letters (1974), (39), 3519-22

CODEN: TELEAY; ISSN: 0040-4039

DOCUMENT TYPE:

Journal English

LANGUAGE:

For diagram(s), see printed CA Issue. GI

Thermal and photochem. ring contraction of the 4-azidoketo steroids I (X =X1 = H2, R2R3 = O or R2 = OAc, R3 = H; X = H2, X1 = CH2, R2 = MeCO, R3 = CH2OAc; X = O, X1 = H2, R2 = AcOCH2CO, R3 = OH) gave the corresponding 5β -cyano-A-norsteroids II. The structure of II (X = X1 = H2, R2R3 = O) was confirmed by x-ray anal. The orthorhombic crystals, space group P212121, had a 11.70, b 12.89, c 10.89, and Z = 4. The structure was solved by direct phase determining procedures and refined by full-matrix least-squares calcns. to R 0.107 for 1282 reflections.

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